

Replication of Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes (PLATO Trial)

January 13, 2020

1. RCT Details

This section provides a high-level overview of the RCT that the described real-world evidence study is trying to replicate as closely as possible given the remaining limitations inherent in the healthcare databases.

1.1 Title

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes ([PLATO](#) trial)

1.2 Intended aim(s)

Compared ticagrelor (180-mg loading dose, 90 mg twice daily thereafter) and clopidogrel (300-to-600-mg loading dose, 75 mg daily thereafter) for the prevention of cardiovascular events in 18,624 patients admitted to the hospital with an acute coronary syndrome, with or without ST-segment elevation.

1.3 Primary endpoint for replication and RCT finding

a composite of death from vascular causes, myocardial infarction, or stroke

1.4 Required power for primary endpoint and noninferiority margin (if applicable)

Estimated that 1780 such events would be required to achieve 90% power to detect a relative risk reduction of 13.5% in the rate of the primary end point in the ticagrelor group as compared with the clopidogrel group, given an event rate of 11% in the clopidogrel group at 12 months.

1.5 Primary trial estimate targeted for replication

HR = 0.84 (95% CI 0.77–0.92) comparing ticagrelor to clopidogrel (Wallentin et al., 2009)

2. Person responsible for implementation of replication in Aetion

Ajinkya Pawar, Ph.D. implemented the study design in the Aetion Evidence Platform. S/he is not responsible for the validity of the design and analytic choices. All implementation steps are recorded and the implementation history is archived in the platform.

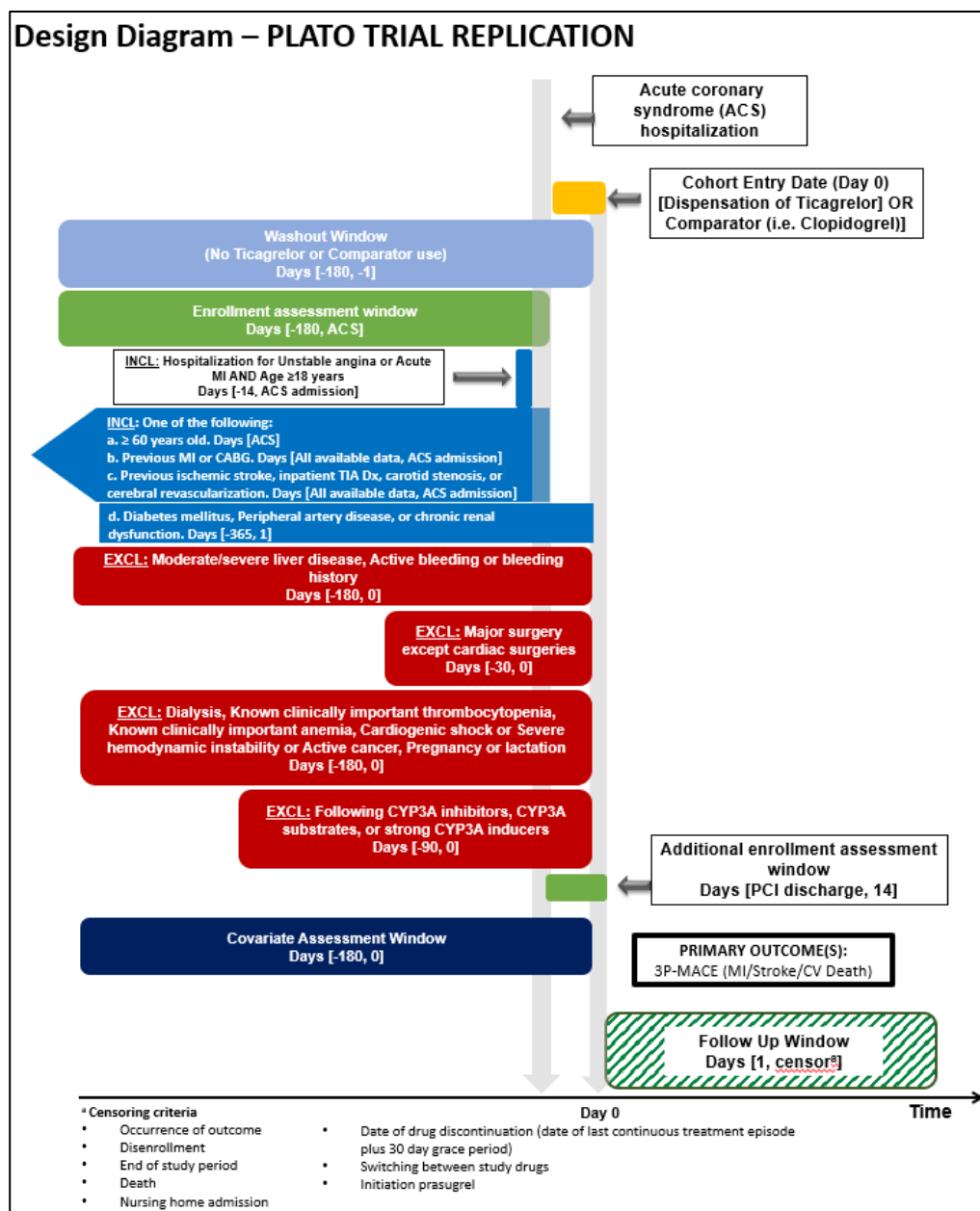
3. Data Source(s)

United/Optum, MarketScan

4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.

Design Diagram – PLATO TRIAL REPLICATION



5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, cohort study design comparing ticagrelor 90mg twice daily to clopidogrel 75mg daily. The patients will be required to have continuous enrollment during the baseline period of 180 days before initiation of ticagrelor 90mg or the comparator drug (cohort entry date). Follow-up for the outcome (3P-MACE), begins the day after drug initiation.

5.2 Important steps for cohort formation

New users (defined as no use in 180 days prior to index date) of an exposure and a comparator drug will be identified.

5.2.1 Eligible cohort entry dates

Market availability of ticagrelor in the U.S. started on 2011-07-20.

- For MarketScan: 2011-07-20 to 2017-12-31 (end of data availability).
- For Optum: 2011-07-20 to 2019-03-31 (end of data availability).

5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in **Appendix A** and are summarized in the flowcharts below.

5.3 Flowchart of the study cohort assembly

	Optum		MarketScan	
	Less Excluded Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
Less Excluded Patients				
All patients		75,524,500		191,990,035
Met cohort entry criteria: Patients with hospitalization for potential ST-segment elevation or non-ST segment elevation Acute Coronary Syndrome	-75275676	248,824	-191715444	274,591

Effectiveness research with Real World Data to support FDA's regulatory decision making

Patients with sufficient enrollment period in the claims database	-33452	215,372	-67391	207,200
Parent: Excluded based on Start of Clopidogrel 75mg OR Ticagrelor 90mg (if never began 14 days after discharge)	-136791	78,581	-119212	87,988
Parent: Excluded based on Enrollment with allowed gap- from hospital discharge to 14 days after discharge	-610	77,971	-1431	86,557
Parent: Final cohort		77,971		86,557
Patients who initiate clopidogrel 75mg or ticagrelor 90mg 14 days within discharge from the ACS hospitalization	-245	77,726	-23	86,534
Patients with sufficient enrollment period covering post 14 days hospital discharge.	0	77,726	0	86,534
Patients with no prior use of clopidogrel	-5415	72,311	-4841	81,693
Patients with no prior use of ticagrelor	-842	71,469	-799	80,894
Patients without qualification in >1 exposure category	-46	71,423	-44	80,850
Patients with age 18 or older	0	71,423	-1	80,849
Patients with risk factors such as age >=60, previous MI, CABG, TIA, Carotid stenosis, cerebral revascularizations, diabetes mellitus, peripheral artery disease, chronic renal dysfunction	-16839	54,584	-22689	58,160
Patients without contraindication to clopidogrel: moderate/severe liver disease 180 days prior to drug initiation	-3508	51,076	-2609	55,551
Patients without contraindication to clopidogrel: active bleeding or bleeding history 180 days prior to drug initiation	-978	50,098	-2631	52,920
Patients without contraindication to clopidogrel: major surgery 30 days prior to drug initiation	-549	49,549	-482	52,438
Patients not on concomitant oral/IV therapy with CYP3A inhibitors 90 days prior to drug initiation	-1011	48,538	-1010	51,428
Patients who do not require dialysis 180 days prior to drug initiation	-654	47,884	-457	50,971
Patients without clinically significant thrombocytopenia 180 days prior to drug initiation	-1108	46,776	-1396	49,575
Patients without clinically significant anemia 180 days prior to drug initiation	-3559	43,217	-4869	44,706
Excluded based on Exclusion #11 - Any other condition that may put the patient at risk- 180 days prior to drug initiation Patients without conditions that put individuals at risk or influence study results such as cardiogenic shock, severe hemodynamic instability, or active cancer 180 days prior to drug initiation.	-1764	41,453	-3848	40,858
Excluded based on Exclusion #13 - Pregnancy- 180 days prior to drug initiation Patients not pregnant	-7	41,446	-9	40,849

Final cohort		41,446		40,849
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6. Variables

6.1 Exposure-related variables:

Study drug:

The study exposure of interest is initiation of ticagrelor. Initiation will be defined as starting treatment with ticagrelor or a comparator drug with no prior use of the corresponding drug in the past 6 months (washout period).

Comparator agents:

- Initiators of ticagrelor 90mg will be compared to initiators of-
 - Clopidogrel 75mg

6.2 Preliminary covariates:

- Age
- Sex
- Combined Comorbidity Index (CCI), measured over the default baseline covariate assessment period, defined as 180 days prior to and including index date

Covariates listed above represent only a small subset of covariates that will ultimately be controlled for in the design and analysis. We use the covariates above only for initial feasibility analyses to judge whether there is likely to be sufficient overlap between treatment groups to proceed with the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and the initial power assessment and are listed in Table 1 (**Appendix B**).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcomes of interest (definitions provided in **Appendix A**):

- **Primary outcome:** 3-point major adverse cardiovascular events (MACE), i.e., non-fatal myocardial infarction, non-fatal stroke, or CV mortality
- Secondary outcomes: Individual components:
 - Hospital admission for MI (for purposes of this individual component, fatal MI is included)
 - Hospital admission for stroke (for purposes of this individual component, fatal stroke is included)
 - All-cause mortality/CV mortality:
 - All-cause inpatient mortality identified using discharge status codes will be used as a proxy for “CV mortality” in MarketScan
 - In Optum, all-cause inpatient mortality + all-cause mortality for Medicare Advantage patients is used

Control outcome of interest (control outcomes only serve to assess aspects of study validity but are not further interpreted):

1. Major bleeding (we expect to see a null association; Wallentin et al., 2009)
2. Pneumonia (we expect to see a null association)

Control outcome definition

Outcome	Definition	Comments
Control Outcomes		
Major bleeding	Any inpatient diagnosis of major bleeding -- code list provided in Appendix A	Same code list used for both outcome and major bleed exclusion criteria
Pneumonia	Any inpatient diagnosis of pneumonia: * 481 - PNEUMOCOCCAL PNEUMONIA [STREPTOCOCCUS PNEUMONIAE PNEUMONIA] * 482 - OTHER BACTERIAL PNEUMONIA * 483 - PNEUMONIA DUE TO OTHER SPECIFIED ORGANISM * 485 - BRONCHOPNEUMONIA ORGANISM UNSPECIFIED * 486 - PNEUMONIA ORGANISM UNSPECIFIED * 487.0 - INFLUENZA WITH PNEUMONIA * 507 - PNEUMONITIS DUE TO SOLIDS AND LIQUIDS * 482.0 - PNEUMONIA DUE TO KLEBSIELLA PNEUMONIAE * 482.1 - PNEUMONIA DUE TO PSEUDOMONAS * 482.2 - PNEUMONIA DUE TO HEMOPHILUS INFLUENZAE * 482.3 - PNEUMONIA DUE TO STREPTOCOCCUS * 482.30 - PNEUMONIA DUE TO STREPTOCOCCUS UNSPECIFIED * 482.31 - PNEUMONIA DUE TO STREPTOCOCCUS GROUP A * 482.32 - PNEUMONIA DUE TO STREPTOCOCCUS GROUP B	PPV = 85% (Aronsky, et al.; 2005); <u>Note-</u> The corresponding ICD-10 codes will also be used

	<ul style="list-style-type: none"> * 482.39 - PNEUMONIA DUE TO OTHER STREPTOCOCCUS * 482.4 - PNEUMONIA DUE TO STAPHYLOCOCCUS * 482.40 - PNEUMONIA DUE TO STAPHYLOCOCCUS UNSPECIFIED * 482.41 - METHICILLIN SUSCEPTIBLE PNEUMONIA DUE TO STAPHYLOCOCCUS AUREUS * 482.42 - METHICILLIN RESISTANT PNEUMONIA DUE TO STAPHYLOCOCCUS AUREUS * 482.49 - OTHER STAPHYLOCOCCUS PNEUMONIA * 482.8 - PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA * 482.81 - PNEUMONIA DUE TO ANAEROBES * 482.82 - PNEUMONIA DUE TO ESCHERICHIA COLI [E.COLI] * 482.83 - PNEUMONIA DUE TO OTHER GRAM-NEGATIVE BACTERIA * 482.84 - PNEUMONIA DUE TO LEGIONNAIRES' DISEASE * 482.89 - PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA * 482.9 - BACTERIAL PNEUMONIA UNSPECIFIED * 483.0 - PNEUMONIA DUE TO MYCOPLASMA PNEUMONIAE * 483.1 - PNEUMONIA DUE TO CHLAMYDIA * 483.8 - PNEUMONIA DUE TO OTHER SPECIFIED ORGANISM * 507.0 - PNEUMONITIS DUE TO INHALATION OF FOOD OR VOMITUS * 507.1 - PNEUMONITIS DUE TO INHALATION OF OILS AND ESSENCES * 507.8 - PNEUMONITIS DUE TO OTHER SOLIDS AND LIQUIDS 	
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6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analyses will be conducted with treatment defined as the index drug on the day of cohort entry. Because adherence in the real-world databases is expected to be much worse than in the trial, the AT analysis is the **primary** analysis, as it targets the relative hazard of outcomes on treatment.

For the AT analyses, the follow-up will start the day after initiation of ticagrelor and comparator and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest, unless otherwise specified for selected outcomes,
- The date of end of continuous registration in the database,
- End of the study period,
- Measured death event occurs,
- Nursing home admission
 - Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.

- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (ticagrelor and comparator) plus a defined grace period (i.e., 30 days after the end of the last prescription's days' supply in main analyses).
- The date of augmentation or switching from an exposure to a comparator.
- Initiation of prasugrel

For the ITT analyses, the censoring based on the augmentation/switching and treatment discontinuation will be replaced with a maximum allowed follow-up time of 365 days.

7. Initial Feasibility Analysis

Aetion report links:

Optum: <https://bwh-dope.aetion.com/projects/details/948/results/45952/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/949/results/45949/result/0>

Date conducted: December 12, 2019

Complete Aetion feasibility analysis using age, sex, and CCI as the only covariates and the primary endpoint (Section 6.3.1) as the outcome. No measures of association will be computed nor will incidence rates stratified by treatment group.

- Report patient characteristics by treatment group
- Report summary parameters of the overall study population
- Report median follow-up time by treatment group
- Report reasons for censoring in the overall study population

8. Initial Power Assessment

Aetion report links:

Optum: <https://bwh-dope.aetion.com/projects/details/948/results/45953/result/6>

Marketscan: <https://bwh-dope.aetion.com/projects/details/949/results/45950/result/6>

Date conducted: December 12, 2019

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, sex, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, sex, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

Reviewed by PI:	Jessica Franklin	Date reviewed:	12/16/2019
Reviewed by FDA:	Ken Quinto	Date reviewed:	1/3/2020
Reasons for stopping analysis (if required):			

9. Balance Assessment after PS matching

Action report links (Ticagrelor vs. clopidogrel):

Optum: <https://bwh-dope.aetion.com/projects/details/948/results/46989/result/0>

Marketscan: <https://bwh-dope.aetion.com/projects/details/949/results/46990/result/0>

Date conducted: 01/05/2020

After review of initial feasibility and power analyses, complete creation of the remaining covariates (see Table 1 below for list of covariates). Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates (excluding laboratory values, which are missing in some patients).

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

	Overall	Referent	Exposure
Dummy Outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	194 (0.69%)	108 (0.77%)	86 (0.62%)
Start of an additional exposure	3,375 (12.07%)	254 (1.82%)	3,121 (22.32%)
End of index exposure	11,280 (40.34%)	5,799 (41.48%)	5,481 (39.21%)
Specified date reached	5,755 (20.58%)	3,626 (25.94%)	2,129 (15.23%)
End of patient enrollment	5,042 (18.03%)	3,039 (21.74%)	2,003 (14.33%)
Switch to Prasugrel (for censoring) + nursing home admission	2,314 (8.28%)	1,154 (8.25%)	1,160 (8.30%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]		
Patient Group	Optum	Marketscan
Overall Patient Population	163 [58-387]	219 [85-409]
Referent	228 [81-444]	259 [113-451]
Exposure	114 [40-310]	179 [59-381]

- Report overall risk of the primary outcome.

	Optum	Marketscan
Risk per 1,000 patients (MACE)	75.73	56.46

10. Final Power Assessment

Date conducted:

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8. If the study is to be implemented in more than one database, copy and paste excel sheet to report power for each database separately and for the pooled analysis that uses data from all databases together. Power calculations are based on the formulas from Chow et al. (2008).

- Pooled

- **For ticagrelor 90mg vs. clopidogrel 75mg (Primary outcome- MACE)**

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	13,980	Reference	13,980
Exposed	13,980	Exposed	13,980
Risk per 1,000 patients	66.10	Risk per 1,000 patients	66.10
Desired HR from RCT	0.865	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1848.156	Number of events expected	1848.156
Power	0.876441293	Power	0.999883191

- Optum

- **For ticagrelor 90mg vs. clopidogrel 75mg (Primary outcome- MACE)**

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	6,697	Reference	6,697
Exposed	6,697	Exposed	6,697
Risk per 1,000 patients	75.73	Risk per 1,000 patients	75.73
Desired HR from RCT	0.865	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	1014.32762	Number of events expected	1014.32762
Power	0.636639088	Power	0.986722295

○ MarketScan

▪ **For ticagrelor 90mg vs. clopidogrel 75mg (Primary outcome- MACE)**

Superiority Analysis		Non-inferiority Analysis	
Number of patients matched		Number of patients matched	
Reference	7,283	Reference	7,283
Exposed	7,283	Exposed	7,283
Risk per 1,000 patients	56.46	Risk per 1,000 patients	56.46
Desired HR from RCT	0.865	Assumed HR from RCT	1
Alpha (2-sided)	0.05	Alpha (2-sided)	0.05
		Non-inferiority margin	1.3
Number of events expected	822.39636	Number of events expected	822.39636
Power	0.54759547	Power	0.964227735

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board. Reviewers evaluate the results of the analyses described above in Sections 9 and 10, including numbers of patients, balance in patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power.

Reviewed by PI:	Jessica Franklin	Date reviewed:	12/16/2019
Reviewed by FDA:	Ken Quinto	Date reviewed:	01/03/2020
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns: 1/10/20

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the individual respondent.

12. Register study protocol on clinicalTrials.gov

Date conducted:

- Register the study on [clinicalTrials.gov](#) and upload this document.

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For **primary analysis**:

- In the PS-matched cohort from Section 9, calculate the HR for each outcome for ticagrelor versus clopidogrel patients using a Cox proportional hazards model.

13.2 For secondary analyses:

- In both pre-matched cohorts, perform asymmetrical trimming to remove patients with PS values below the 2.5th percentile of treated patients and above the 97.5th percentile of untreated patients. In the trimmed cohort, calculate the HR for ticagrelor versus referent patients using a Cox proportional hazards model, adjusting for deciles of the PS.

14. Requested Results

14.1 Results from primary and secondary analyses;

Analysis	No. exposed events	No. referent events	Exposed rate	Referent rate	HR (95% CI)
Crude					
Primary analysis					
Analysis 2					
...					

HR, Hazard Ratio; CI, Confidence Interval.

15. References

Aronsky, Dominik, et al. Accuracy of Administrative Data for Identifying Patients with Pneumonia. American Journal of Medical Quality. 2005; 20(6);319–28. doi:10.1177/1062860605280358.

Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. **page 177**

Wallentin L, Becker RC, Budaj A, et al. N Engl J Med 2009; 361:1045-1057

Appendix A

#	PLATO trial definitions	Implementation in routine care	References/Rationale	Color coding
	Trial details- Hazard Ratio, 0.84; 95% confidence interval [CI], 0.77 to 0.92)		Please see the following Google Drive for further details or any missing information: https://drive.google.com/open?id=1WD618wqyYfFaXrLI7cuK-V0cnh6b-gV	Adequate mapping in claims
	EXPOSURE vs. COMPARISON		Not all ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd-10-cm-and-cc-crosswalk-general-equivalence-mapping.html	Intermediate mapping in claims
	Ticagrelor (90 mg twice daily) vs Clopidogrel (75mg daily)	Exposure) Ticagrelor Reference) Clopidogrel	KEY TIME POINTS: Index event: Onset of Acute coronary syndrome (ACS) which becomes the indication for study drug (ticagrelor or clopidogrel) initiation Index hospitalization: Hospitalization for the treatment of index event Drug Initiation date: New prescription claim for the study drug in patients with a record of index hospitalization in the previous 2 weeks. * We assume that the patient first initiates study drug in hospital and continues to be part of the initiator group as long as a prescription is filled within 2 weeks of discharge of ACS event.	Poor mapping or cannot be measured in claims
	PRIMARY OUTCOME			Can't be measured in claims but not important for the analysis
	The primary efficacy end point is time to first occurrence of death from vascular causes, myocardial infarction, or stroke.	Measured 1 day after drug initiation in diagnosis position specified below and inpatient care setting: Inpatient mortality/MI/Stroke For MI Any diagnosis position in inpatient care setting ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care) For stroke Primary diagnosis position in inpatient care setting ICD-9 discharge diagnosis: 430.xx Subarachnoid hemorrhage (SAH) 431.xx Intracerebral hemorrhage (ICH) 433.x1 Occlusion and stenosis of precerebral arteries with cerebral infarction 434.xx (excluding 434.x0) Occlusion and stenosis of cerebral arteries with cerebral infarction 436.x Acute, but ill-defined cerebrovascular events Mortality- See Mortality Sheet.	For MI: →PPV 94% in Medicare claims data [Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH. Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records. American heart journal 2004;148:99-104.] →PPV 88.4% in commercially-insured population [Wahl PM, Rodgers K, Schneeweiss S, et al. Validation of claims-based diagnostic and procedure codes for cardiovascular and gastrointestinal serious adverse events in a commercially-insured population. Pharmacoepidemiology and Drug Safety 2010;19:596-603.] For stroke: PPV of 85% or higher for ischemic stroke PPV ranging from 80% to 98% for hemorrhagic stroke →[Andrade SE, Harrold LR, Tjia J, et al. A systematic review of validated methods for identifying cerebrovascular accident or transient Ischemic attack using administrative data. Pharmacoepidemiology and Drug Safety 2012;21 Suppl 1:100-28.] →[Tirschwell DL, Longstreth WT, Jr. Validating administrative data in stroke research. Stroke; a journal of cerebral circulation 2002;33:2465-70.] →[Rounie CL, Mitchell E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. Pharmacoepidemiology and drug safety 2008;17:20-6.]	
	INCLUSION CRITERIA			
	1-4 ALL FOUR ARE REQUIRED			
1	Hospitalized for potential ST-segment elevation or non-ST-segment elevation ACS, with onset during the previous 24 hours, documented by cardiac ischemic symptoms due to atherosclerosis of ≥10 minutes' duration at rest	Measured 2 weeks prior to index hospitalization in inpatient, primary diagnosis position Acute MI: ICD-9 Dx 410.X (acute myocardial infarction) excluding 410.x2 (subsequent episode of care) ICD-10: I21.0x, I21.1x, I21.2x, I21.3x, I21.4x, I22.0x, I22.1x, I22.2x, I22.8x, I22.9x, I25.2x Unstable angina: ICD-9: 411.x ICD-10: I24.1x, I20.0x, I25.1x, I25.7x, I24.0x, I24.8x, I24.9x		
2	≥18 years of age	Measured at Index hospitalization Age ≥=18		
3	Not pregnant. Urinary and/or blood pregnancy tests are to be performed in women of child-bearing potential and repeated at least every 6 months. Women of child-bearing potential must be using ≥2 forms of reliable contraception, including one barrier method.	Please see exclusion #13		
4	With informed consent	N/A		
	IN ADDITION TO 1-4, MEET CRITERIA 5A OR 5B			
5A	≥2 of the following 3 risk factors	* Note) In the claims, we are unable to measure ≥2 of the 3 risk factors		
	1. ST-segment changes on ECG indicating ischemia. ST-segment depression or transient elevation ≥ 1 mm in two or more 2 contiguous leads	N/A		

Appendix A

	2. Positive biomarker indicating myocardial necrosis. Troponin I or T or CK-MB greater than the upper limit of normal	N/A	
	3. One of the following:		
	(a) ≥60 y of age	Measured at Index hospitalization Age ≥= 60	
	(b) Previous MI or CABG	Measured any time prior to Index hospitalization In any diagnosis position and Inpatient or outpatient care setting as defined below: MI: ICD-9 Acute MI: 410.xx, Old MI: 412.xx CABG: Inpatient CPT-4: 33510 – 33536, 33545, 33572. Or Inpatient or outpatient ICD-9 procedure: 36.1x, 36.2x	Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	(c) CAD with ≥50% stenosis in ≥2 vessels	N/A	
	(d) Previous ischemic stroke, TIA (hospital-based diagnosis), carotid stenosis (≥50%), or cerebral revascularization	Measured any time prior to Index hospitalization In any diagnosis position and Inpatient or outpatient care setting as defined below: (exception: TIA - Inpatient diagnosis only) Ischemic stroke: ICD-9: 433.x, 434. x TIA (Inpatient diagnosis, any position) : ICD-9 : 435.xx Carotid stenosis: ICD-9: 433.1x Cerebral revascularization: ICD-9 procedure code Carotid endarterectomy (38.12). Angioplasty/atherectomy of precerebral vessels (00.61) Carotid artery stenting (00.63).	Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	(e) Diabetes mellitus	Measured 365 days prior to drug Initiation In any diagnosis position and Inpatient or outpatient care setting as defined below: Diabetes type 1: ICD-9 : 250.x1 or 250.x ICD-10: E10.x Diabetes type 2: ICD-9: 250.x0 or 250.x2 ICD-10 E11.x	Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	(f) Peripheral artery disease	Measured 365 days prior drug Initiation In any diagnosis position and Inpatient or outpatient care setting as defined below: Peripheral vascular disease ICD-9: 440.20 – 440.24, 440.29 – 440.32, 440.3, 440.4, 443.9	Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	(g) Chronic renal dysfunction	Measured 365 days prior to drug Initiation In any diagnosis position and Inpatient or outpatient care setting as defined below: Chronic kidney disease: ICD-9: 585.3x-585.6x	Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119 Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177
	OR		
58	Persistent ST-segment elevation ≥1 mm (not known to be preexisting or due to a coexisting disorder) in ≥2 contiguous leads or new LBBB plus primary PCI planned.	N/A	
	EXCLUSION CRITERIA		
	Drug related		

Appendix A

1	1. Contraindication to clopidogrel or other reason that study drug should not be administered (eg, hypersensitivity, moderate or severe liver disease, active bleeding or bleeding history, major surgery within 30 days)	<p>Moderate/severe liver disease: Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting ICD-9 diagnosis codes: 070.xx, 570.xx- 573.xx 456.0x-456.2x, 576.8x, 782.4x, 789.5x ICD-9 procedure codes: 39.1x, 42.91</p> <p>Active bleeding or bleeding history: Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Codes are in the sheet 'Major Bleeding'</p> <p>Major surgery (except cardiac surgeries): Measured 30 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Major surgery selected from ICD-9 procedure codes range 40.x- 84.x (procedures 35.x -39.x [cardiovascular procedures] are excluded)</p>	<p>Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
2	2. Oral anticoagulation therapy that cannot be stopped	N/A	
3	3. Fibrinolytic therapy planned or within the previous 24 h	N/A	
4	4. Concomitant oral or IV therapy with strong CYP3A inhibitors (ketoconazole, itraconazole, voriconazole, telithromycin, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir, grapefruit juice N1 L/d), CYP3A substrates with narrow therapeutic indices (cyclosporine, quinidine), or strong CYP3A inducers (rifampin/rifampicin, phenytoin, carbamazepine)	<p>Prescription claim for following CYP3A inhibitors, CYP3A substrates, or strong CYP3A Inducers Measured 90 days prior to drug initiation</p> <p>Ketoconazole, itraconazole, voriconazole, telithromycin, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir Cyclosporine, quinidine Rifampin, rifampicin/rifampin, phenytoin, carbamazepine</p>	
Treatment Related			
5	1. Index event is an acute complication of PCI	N/A	
6	2. PCI after index event and before first study dose	N/A	
Medical Related			
7	1. Increased risk of bradycardiac events	N/A	
8	2. Dialysis required	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Codes are in the sheet 'Dialysis'</p>	<p>Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi:</p>
9	3. Known clinically important thrombocytopenia	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Thrombocytopenia ICD-9: 287.3x, 287.4x, 287.5x</p>	
10	4. Known clinically important anemia	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting Anemia (unspecified anemia including anemia of chronic illness, sideroblastic anemia) ICD-9: 285.x</p>	
11	5. Any other condition that may put the patient at risk or influence study results in the investigators' opinion (eg, cardiogenic shock, severe hemodynamic instability, active cancer)	<p>Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting</p> <p>Cardiogenic shock: ICD-9: 785.51</p> <p>Severe hemodynamic instability: ICD-9: 785.59 Other shock without mention of trauma 785.52 Septic shock 785.50 shock, unspecified</p> <p>Active cancer: ICD-9: History of malignant neoplasm 140.xx-208.xx (except 173.xx, non-melanoma skin cancer)</p>	<p>Patomo, Elisabetta et al. "Cardiovascular outcomes associated with canagliflozin versus other non-gliiflozin antidiabetic drugs: population based cohort study." BMJ 2018;360:k119 http://dx.doi.org/10.1136/bmj.k119</p> <p>Patomo, Elisabetta et al. "Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care: A First Analysis from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study." Circulation. 2019 Apr 8. doi: 10.1161/CIRCULATIONAHA.118.039177</p>
General			
12	1. Participant in another investigational drug or device study within 30 days	N/A	

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13	2. Pregnancy or lactation	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting	
14	3. Any condition that increases the risk for noncompliance or being lost to follow-up	Codes are in the sheet "Pregnancy"	
15	4. Involvement in the planning or conduct of the study	N/A	
16	5. Previous enrollment or randomization in this study	N/A	

Appendix A

<u>Trial ID</u>	pNDA10
<u>Trial Name (with web links)</u>	PLATO
<u>Trial Name (with pdf links)</u>	PLATO
<u>NCT</u>	NCT00391872
<u>Trial category</u>	Primary indication
<u>Run-in period Description</u>	
<u>Run-in period</u>	
<u>Therapeutic Area</u>	Cardiology/Vascular Diseases
<u>Study batch</u>	Antiplatelets
<u>RCT Category</u>	1a- Intended S with label change
<u>Brand Name</u>	Brilinta
<u>Generic Name</u>	ticagrelor
<u>Sponsor</u>	AstraZeneca
<u>Year</u>	2011
<u>Measurable endpoint</u>	Primary composite endpoint of cardiovascular death, non-fatal MI (excluding silent MI), or non-fatal stroke
<u>Exposure</u>	Ticagrelor
<u>Comparator</u>	Clopidogrel
<u>Population</u>	Patients admitted to the hospital with an acute coronary syndrome, with or without ST-segment elevation. 89% patients on Beta-blocker, 76% ACE inhibitors, 89% on statins
<u>Trial finding</u>	RR = 0.84 (95% CI 0.77–0.92)
<u>Notes</u>	
<u>No. of Patients</u>	18,624
<u>Non-inferiority margin</u>	-
<u>Assay Sens. Outcome</u>	
<u>Assay Sens. Endpoint (from trial)</u>	

Appendix A

<u>Finding for potential Assay Sens. Outcome from trial-</u>	
<u>Power</u>	0.90 to detect a relative risk reduction of 13.5% in the rate of the primary end point
<u>Blinding</u>	Double-blinded
<u>Statistical Method</u>	
<u>Approval indication</u>	For the reduction of thrombotic events in patients with acute coronary syndrome

Appendix A

Mortality- Dependent on data source.

1. All-cause mortality / inpatient mortality

Identified using the vital status file-

Medicare

Identified using the discharge status codes-

Optum-

- 20 = EXPIRED
- 21 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 22 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 23 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 24 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 25 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 26 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 27 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 28 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 29 = EXPIRED TO BE DEFINED AT STATE LEVEL
- 40 = EXPIRED AT HOME (HOSPICE)
- 41 = EXPIRED IN A MEDICAL FACILITY (HOSPICE)
- 42 = EXPIRED - PLACE UNKNOWN (HOSPICE)

Truven-

- 20 - Died
- 22 - Died
- 23 - Died
- 24 - Died
- 25 - Died
- 26 - Died
- 27 - Died
- 28 - Died
- 29 - Died
- 40 - Other died status or Expired at home (Hospice claims only) (depends on year)
- 41 - Other died status or Expired in medical facility (Hospice claims only) (depends on year)

Appendix A

- 42 - Other died status or Expired - place unknown (Hospice claims only) (depends on year)
- 21 - Died or Disch./Transf. to court/law enforcement (depends on year)

2. CV mortality

Information on CV mortality through data linkage with the National Death Index (NDI) will be available for Medicare at a later date. We will conduct secondary analyses using CV mortality at that time.

Appendix A

Major bleeding control outcome: 1 inpatient (any position)	
Major bleeding exclusion criteria: 1 inpatient (any position) or 2 outpatient diagnosis (separated by 7-365 days)	
562.02	(ICD9) DIVERTICULOSIS OF SMALL INTESTINE WITH HEMORRHAGE
562.03	(ICD9) DIVERTICULITIS OF SMALL INTESTINE WITH HEMORRHAGE
562.12	(ICD9) DIVERTICULOSIS OF COLON WITH HEMORRHAGE
562.13	(ICD9) DIVERTICULITIS OF COLON WITH HEMORRHAGE
568.81	(ICD9) HEMOPERITONEUM (NONTRAUMATIC)
569.3	(ICD9) HEMORRHAGE OF RECTUM AND ANUS
569.83	(ICD9) PERFORATION OF INTESTINE
569.85	(ICD9) ANGIODYSPLASIA OF INTESTINE WITH HEMORRHAGE
569.86	(ICD9) DIEULAFOY LESION (HEMORRHAGIC) OF INTESTINE
578	(ICD9) HEMATEMESIS
578.9	(ICD9) HEMORRHAGE OF GASTROINTESTINAL TRACT UNSPECIFIED
423	(ICD9) HEMOPERICARDIUM
432	(ICD9) NONTRAUMATIC EXTRADURAL HEMORRHAGE
432.1	(ICD9) SUBDURAL HEMORRHAGE
432.9	(ICD9) UNSPECIFIED INTRACRANIAL HEMORRHAGE
459	(ICD9) HEMORRHAGE UNSPECIFIED
531	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE
531	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
531.01	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
531.2	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
531.2	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
531.21	(ICD9) ACUTE GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
531.4	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE
531.4	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
531.41	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE WITH OBSTRUCTION
531.6	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION
531.6	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
531.61	(ICD9) CHRONIC OR UNSPECIFIED GASTRIC ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
532	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE
532	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
532.01	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
532.2	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION

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532.2	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
532.21	(ICD9) ACUTE DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
532.4	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE
532.4	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
532.41	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
532.6	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION
532.6	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
532.61	(ICD9) CHRONIC OR UNSPECIFIED DUODENAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
533	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
533	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
533.01	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
533.2	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION
533.2	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
533.21	(ICD9) ACUTE PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
533.4	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE
533.4	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITHOUT OBSTRUCTION
533.41	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE WITH OBSTRUCTION
533.6	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION
533.6	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
533.61	(ICD9) CHRONIC OR UNSPECIFIED PEPTIC ULCER OF UNSPECIFIED SITE WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
534	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE
534	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
534.01	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
534.2	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION
534.2	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
534.21	(ICD9) ACUTE GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
534.4	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE
534.4	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITHOUT OBSTRUCTION
534.41	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE WITH OBSTRUCTION
534.6	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION
534.6	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITHOUT OBSTRUCTION
534.61	(ICD9) CHRONIC OR UNSPECIFIED GASTROJEJUNAL ULCER WITH HEMORRHAGE AND PERFORATION WITH OBSTRUCTION
578.1	(ICD9) BLOOD IN STOOL
719.1	(ICD9) HEMARTHROSIS
719.1	(ICD9) HEMARTHROSIS SITE UNSPECIFIED

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719.11	(ICD9) HERARTHROSIS INVOLVING SHOULDER REGION
719.12	(ICD9) HEMARTHORSIS INVOLVING UPPER ARM
719.13	(ICD9) HEMARTHROSIS INVOLVING FOREARM
719.14	(ICD9) HEMARTHROSIS INVOLVING HAND
719.15	(ICD9) HEMARTHROSIS INVOLVING PELVIC REGION AND THIGH
719.16	(ICD9) HEMARTHROSIS INVOLVING LOWER LEG
719.17	(ICD9) HEMARTHROSIS INVOLVING ANKLE AND FOOT
719.18	(ICD9) HEMARTHROSIS INVOLVING OTHER SPECIFIED SITES
719.19	(ICD9) HEMARTHROSIS INVOLVING MULTIPLE SITES
430	(ICD9) SUBARACHNOID HEMORRHAGE
431	(ICD9) INTRACEREBRAL HEMORRHAGE
I31.2	(ICD10) Hemopericardium, not elsewhere classified
I60.00	(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified carotid siphon and bifurcation
I60.01	(ICD10) Nontraumatic subarachnoid hemorrhage from right carotid siphon and bifurcation
I60.02	(ICD10) Nontraumatic subarachnoid hemorrhage from left carotid siphon and bifurcation
I60.10	(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified middle cerebral artery
I60.11	(ICD10) Nontraumatic subarachnoid hemorrhage from right middle cerebral artery
I60.12	(ICD10) Nontraumatic subarachnoid hemorrhage from left middle cerebral artery
I60.2	(ICD10) Nontraumatic subarachnoid hemorrhage from anterior communicating artery
I60.30	(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified posterior communicating artery
I60.31	(ICD10) Nontraumatic subarachnoid hemorrhage from right posterior communicating artery
I60.32	(ICD10) Nontraumatic subarachnoid hemorrhage from left posterior communicating artery
I60.4	(ICD10) Nontraumatic subarachnoid hemorrhage from basilar artery
I60.50	(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified vertebral artery
I60.51	(ICD10) Nontraumatic subarachnoid hemorrhage from right vertebral artery
I60.52	(ICD10) Nontraumatic subarachnoid hemorrhage from left vertebral artery
I60.6	(ICD10) Nontraumatic subarachnoid hemorrhage from other intracranial arteries
I60.7	(ICD10) Nontraumatic subarachnoid hemorrhage from unspecified intracranial artery
I60.8	(ICD10) Other nontraumatic subarachnoid hemorrhage
I60.9	(ICD10) Nontraumatic subarachnoid hemorrhage, unspecified
I61.0	(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, subcortical
I61.1	(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, cortical
I61.2	(ICD10) Nontraumatic intracerebral hemorrhage in hemisphere, unspecified
I61.3	(ICD10) Nontraumatic intracerebral hemorrhage in brain stem
I61.4	(ICD10) Nontraumatic intracerebral hemorrhage in cerebellum

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I61.5	(ICD10) Nontraumatic intracerebral hemorrhage, intraventricular
I61.6	(ICD10) Nontraumatic intracerebral hemorrhage, multiple localized
I61.8	(ICD10) Other nontraumatic intracerebral hemorrhage
I61.9	(ICD10) Nontraumatic intracerebral hemorrhage, unspecified
I62.00	(ICD10) Nontraumatic subdural hemorrhage, unspecified
I62.01	(ICD10) Nontraumatic acute subdural hemorrhage
I62.02	(ICD10) Nontraumatic subacute subdural hemorrhage
I62.03	(ICD10) Nontraumatic chronic subdural hemorrhage
I62.1	(ICD10) Nontraumatic extradural hemorrhage
I62.9	(ICD10) Nontraumatic intracranial hemorrhage, unspecified
K25.0	(ICD10) Acute gastric ulcer with hemorrhage
K25.2	(ICD10) Acute gastric ulcer with both hemorrhage and perforation
K25.4	(ICD10) Chronic or unspecified gastric ulcer with hemorrhage
K25.6	(ICD10) Chronic or unspecified gastric ulcer with both hemorrhage and perforation
K26.0	(ICD10) Acute duodenal ulcer with hemorrhage
K26.2	(ICD10) Acute duodenal ulcer with both hemorrhage and perforation
K26.4	(ICD10) Chronic or unspecified duodenal ulcer with hemorrhage
K26.6	(ICD10) Chronic or unspecified duodenal ulcer with both hemorrhage and perforation
K27.0	(ICD10) Acute peptic ulcer, site unspecified, with hemorrhage
K27.2	(ICD10) Acute peptic ulcer, site unspecified, with both hemorrhage and perforation
K27.4	(ICD10) Chronic or unspecified peptic ulcer, site unspecified, with hemorrhage
K27.6	(ICD10) Chronic or unspecified peptic ulcer, site unspecified, with both hemorrhage and perforation
K28.0	(ICD10) Acute gastrojejunal ulcer with hemorrhage
K28.2	(ICD10) Acute gastrojejunal ulcer with both hemorrhage and perforation
K28.4	(ICD10) Chronic or unspecified gastrojejunal ulcer with hemorrhage
K28.6	(ICD10) Chronic or unspecified gastrojejunal ulcer with both hemorrhage and perforation
K55.21	(ICD10) Angiodysplasia of colon with hemorrhage
K56.60	(ICD10) Unspecified intestinal obstruction
K57.01	(ICD10) Diverticulitis of small intestine with perforation and abscess with bleeding
K57.11	(ICD10) Diverticulosis of small intestine without perforation or abscess with bleeding
K57.13	(ICD10) Diverticulitis of small intestine without perforation or abscess with bleeding
K57.21	(ICD10) Diverticulitis of large intestine with perforation and abscess with bleeding
K57.31	(ICD10) Diverticulosis of large intestine without perforation or abscess with bleeding
K57.33	(ICD10) Diverticulitis of large intestine without perforation or abscess with bleeding
K57.41	(ICD10) Diverticulitis of both small and large intestine with perforation and abscess with bleeding

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K57.51	(ICD10) Diverticulosis of both small and large intestine without perforation or abscess with bleeding
K57.53	(ICD10) Diverticulitis of both small and large intestine without perforation or abscess with bleeding
K57.81	(ICD10) Diverticulitis of intestine, part unspecified, with perforation and abscess with bleeding
K57.91	(ICD10) Diverticulosis of intestine, part unspecified, without perforation or abscess with bleeding
K57.93	(ICD10) Diverticulitis of intestine, part unspecified, without perforation or abscess with bleeding
K62.5	(ICD10) Hemorrhage of anus and rectum
K63.1	(ICD10) Perforation of intestine (nontraumatic)
K63.81	(ICD10) Dieulafoy lesion of intestine
K66.1	(ICD10) Hemoperitoneum
K92.0	(ICD10) Hematemesis
K92.1	(ICD10) Melena
K92.2	(ICD10) Gastrointestinal hemorrhage, unspecified
M25.00	(ICD10) Hemarthrosis, unspecified joint
M25.011	(ICD10) Hemarthrosis, right shoulder
M25.012	(ICD10) Hemarthrosis, left shoulder
M25.019	(ICD10) Hemarthrosis, unspecified shoulder
M25.021	(ICD10) Hemarthrosis, right elbow
M25.022	(ICD10) Hemarthrosis, left elbow
M25.029	(ICD10) Hemarthrosis, unspecified elbow
M25.031	(ICD10) Hemarthrosis, right wrist
M25.032	(ICD10) Hemarthrosis, left wrist
M25.039	(ICD10) Hemarthrosis, unspecified wrist
M25.041	(ICD10) Hemarthrosis, right hand
M25.042	(ICD10) Hemarthrosis, left hand
M25.049	(ICD10) Hemarthrosis, unspecified hand
M25.051	(ICD10) Hemarthrosis, right hip
M25.052	(ICD10) Hemarthrosis, left hip
M25.059	(ICD10) Hemarthrosis, unspecified hip
M25.061	(ICD10) Hemarthrosis, right knee
M25.062	(ICD10) Hemarthrosis, left knee
M25.069	(ICD10) Hemarthrosis, unspecified knee
M25.071	(ICD10) Hemarthrosis, right ankle
M25.072	(ICD10) Hemarthrosis, left ankle
M25.073	(ICD10) Hemarthrosis, unspecified ankle
M25.074	(ICD10) Hemarthrosis, right foot

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M25.075	(ICD10) Hemarthrosis, left foot
M25.076	(ICD10) Hemarthrosis, unspecified foot
M25.08	(ICD10) Hemarthrosis, other specified site
R58	(ICD10) Hemorrhage, not elsewhere classified
R04	(ICD10) Hemorrhage from respiratory passages
R04.0	(ICD10) Epistaxis
R04.1	(ICD10) Hemorrhage from throat
R04.2	(ICD10) Hemoptysis
R04.8	(ICD10) Hemorrhage from other sites in respiratory passages
R04.81	(ICD10) Acute idiopathic pulmonary hemorrhage in infants
R04.89	(ICD10) Hemorrhage from other sites in respiratory passages
R04.9	(ICD10) Hemorrhage from respiratory passages, unspecified
R31	(ICD10) Hematuria
R31.0	(ICD10) Gross hematuria
R31.1	(ICD10) Benign essential microscopic hematuria
R31.2	(ICD10) Other microscopic hematuria
R31.21	
R31.29	
R31.9	(ICD10) Hematuria, unspecified
784.7	(ICD9) EPISTAXIS
784.8	(ICD9) HEMORRHAGE FROM THROAT
599.7	(ICD9) HEMATURIA
599.7	(ICD9) HEMATURIA UNSPECIFIED
599.71	(ICD9) GROSS HEMATURIA
599.72	(ICD9) MICROSCOPIC HEMATURIA
786.3	(ICD9) HEMOPTYSIS
786.3	(ICD9) HEMOPTYSIS UNSPECIFIED
786.31	(ICD9) ACUTE IDIOPATHIC PULMONARY HEMORRHAGE IN INFANTS
786.39	(ICD9) OTHER HEMOPTYSIS
The occurrence of Inpatient with the following attributes:	
Procedure Code (Any Position) is any of: { "44.43", "43255", "0W3P8ZZ" }	
44.43	(ICD9) ENDOSCOPIC CONTROL OF GASTRIC OR DUODENAL BLEEDING
43255	(HCPCS) Esophagogastroduodenoscopy, flexible, transoral; with control of bleeding, any method / Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with control of bleeding, any method
0W3P8ZZ	(ICD10) Control Bleeding in Gastrointestinal Tract, Via Natural or Artificial Opening Endoscopic

Appendix A

Dialysis codes

ESRD, defined as 2 codes (either inpatient or outpatient), separated by at least 30 days

Codes include:

- ICD9 prox codes:

39.95, Hemodialysis

54.98, Peritoneal dialysis

- ICD9 dx codes:

585.5x, Chronic kidney disease, Stage V (for ESRD with no mention of dialysis)

585.6x, End stage renal disease (for ESRD with dialysis)

V56.0x, encounter for dialysis NOS

V56.8x, encounter for peritoneal dialysis

V45.1x, renal dialysis status

- CPT4 codes:

90957, 90960, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 4 or more face-to-face physician visits per month

90958, 90961, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 2-3 face-to-face physician visits per month

90959, 90962, ESRD related services monthly, for patients 12-19 and 20 years of age and older; with 1 face-to-face physician visit per month

90920, 90921, ESRD related services per full month; for patients 12-19 and twenty years of age and over

90924, 90925, ESRD related services (less than full month), per day; for patients 12-19 and twenty years of age and over

90935, Hemodialysis procedure with single physician evaluation

90937, Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription

90945, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single physician evaluation

90947, Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated physician evaluations, with or without substantial revision of dialysis prescription

90965, 90966, ESRD related services for home dialysis per full month, for patients 12-19 and 20 years of age and older

90969, 90970, ESRD related services for dialysis less than a full month of service, per day; for patients 12-19 and 20 years of age and older

90989, Dialysis training, patient, including helper where applicable, any mode, completed course

90993, Dialysis training, patient, including helper where applicable, any mode, course not completed, per training session

90999, Unlisted dialysis procedure, inpatient or outpatient

99512, Home visit for hemodialysis

- HCPCS codes:

G0257, Unscheduled or emergency dialysis treatment for ESRD patient in a hospital outpatient dept. that is not certified as an ESRD facility

G0314, G0317, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/4 or more physician visit per month

G0315, G0318, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/2 or 3 physician visit per month

Appendix A

for the adequacy of nutrition, etc. w/ 1 physician visit per month

G0316, G0319, ESRD related services during the course of treatment, for patients 12-19 and 20 yrs of age and over to include monitoring for the adequacy of nutrition, etc. w/1 physician visit per month

Appendix A

Pregnancy

Dx codes

650 NORMAL DELIVERY
660 OBSTRUCTED LABOR
661 ABNORMALITY OF FORCES OF LABOR
662 LONG LABOR
663 UMBILICAL CORD COMPLICATIONS DURING LABOR AND DELIVERY
664 TRAUMA TO PERINEUM AND VULVA DURING DELIVERY
665 OTHER OBSTETRICAL TRAUMA
667 RETAINED PLACENTA OR MEMBRANES WITHOUT HEMORRHAGE
668 COMPLICATIONS OF THE ADMINISTRATION OF ANESTHETIC OR OTHER SEDATION IN LABOR AND DELIVERY
669.94 UNSPECIFIED COMPLICATION OF LABOR AND DELIVERY POSTPARTUM CONDITION OR COMPLICATION
V24 POSTPARTUM CARE AND EXAMINATION
V24.0 POSTPARTUM CARE AND EXAMINATION IMMEDIATELY AFTER DELIVERY
V24.1 POSTPARTUM CARE AND EXAMINATION OF LACTATING MOTHER
V24.2 ROUTINE POSTPARTUM FOLLOW
V27 OUTCOME OF DELIVERY
V27.0 MOTHER WITH SINGLE LIVEBORN
V27.1 MOTHER WITH SINGLE STILLBORN
V27.2 MOTHER WITH TWINS BOTH LIVEBORN
V27.3 MOTHER WITH TWINS ONE LIVEBORN AND ONE STILLBORN
V27.4 MOTHER WITH TWINS BOTH STILLBORN
V27.5 MOTHER WITH OTHER MULTIPLE BIRTH ALL LIVEBORN
V27.6 MOTHER WITH OTHER MULTIPLE BIRTH SOME LIVEBORN
V27.7 MOTHER WITH OTHER MULTIPLE BIRTH ALL STILLBORN
V27.9 MOTHER WITH UNSPECIFIED OUTCOME OF DELIVERY

Procedure codes

72.0 LOW FORCEPS OPERATION
72.1 LOW FORCEPS OPERATION WITH EPISIOTOMY
72.2 MID FORCEPS OPERATION
72.21 MID FORCEPS OPERATION WITH EPISIOTOMY
72.29 OTHER MID FORCEPS OPERATION
72.3 HIGH FORCEPS OPERATION
72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
72.39 OTHER HIGH FORCEPS OPERATION

Appendix A

- 72.4 FORCEPS ROTATION OF FETAL HEAD
- 72.5 BREECH EXTRACTION
 - 72.51 PARTIAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
 - 72.52 OTHER PARTIAL BREECH EXTRACTION
 - 72.53 TOTAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
 - 72.54 OTHER TOTAL BREECH EXTRACTION
- 72.6 FORCEPS APPLICATION TO AFTERCOMING HEAD
- 72.7 VACUUM EXTRACTION
 - 72.71 VACUUM EXTRACTION WITH EPISIOTOMY
 - 72.79 OTHER VACUUM EXTRACTION
- 72.8 OTHER SPECIFIED INSTRUMENTAL DELIVERY
- 72.9 UNSPECIFIED INSTRUMENTAL DELIVERY
- 73.0 ARTIFICIAL RUPTURE OF MEMBRANES
 - 73.01 INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF MEMBRANES
 - 73.09 OTHER ARTIFICIAL RUPTURE OF MEMBRANES
- 73.1 OTHER SURGICAL INDUCTION OF LABOR
- 73.2 INTERNAL AND COMBINED VERSION AND EXTRACTION
 - 73.21 INTERNAL AND COMBINED VERSION WITHOUT EXTRACTION
 - 73.22 INTERNAL AND COMBINED VERSION WITH EXTRACTION
- 73.3 FAILED FORCEPS
- 73.4 MEDICAL INDUCTION OF LABOR
- 73.5 MANUALLY ASSISTED DELIVERY
 - 73.51 MANUAL ROTATION OF FETAL HEAD
 - 73.59 OTHER MANUALLY ASSISTED DELIVERY
- 73.6 EPISIOTOMY
- 73.8 OPERATIONS ON FETUS TO FACILITATE DELIVERY
- 73.9 OTHER OPERATIONS ASSISTING DELIVERY
 - 73.91 EXTERNAL VERSION ASSISTING DELIVERY
 - 73.92 REPLACEMENT OF PROLAPSED UMBILICAL CORD
 - 73.93 INCISION OF CERVIX TO ASSIST DELIVERY
 - 73.94 PUBIOTOMY TO ASSIST DELIVERY
 - 73.99 OTHER OPERATIONS ASSISTING DELIVERY
- 74.0 CLASSICAL CESAREAN SECTION
 - 74.1 LOW CERVICAL CESAREAN SECTION
 - 74.2 EXTRAPERITONEAL CESAREAN SECTION

Appendix A

74.3	REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY
74.4	CESAREAN SECTION OF OTHER SPECIFIED TYPE
74.9	CESAREAN SECTION OF UNSPECIFIED TYPE
74.91	HYSTEROTOMY TO TERMINATE PREGNANCY
74.99	OTHER CESAREAN SECTION OF UNSPECIFIED TYPE
75.4	MANUAL REMOVAL OF RETAINED PLACENTA
75.5	REPAIR OF CURRENT OBSTETRIC LACERATION OF UTERUS
75.6	REPAIR OF OTHER CURRENT OBSTETRIC LACERATION
75.7	MANUAL EXPLORATION OF UTERINE CAVITY, POSTPARTUM
75.9	OTHER OBSTETRIC OPERATIONS

Appendix B

Optum

MarketScan

BEFORE PS MATCHING

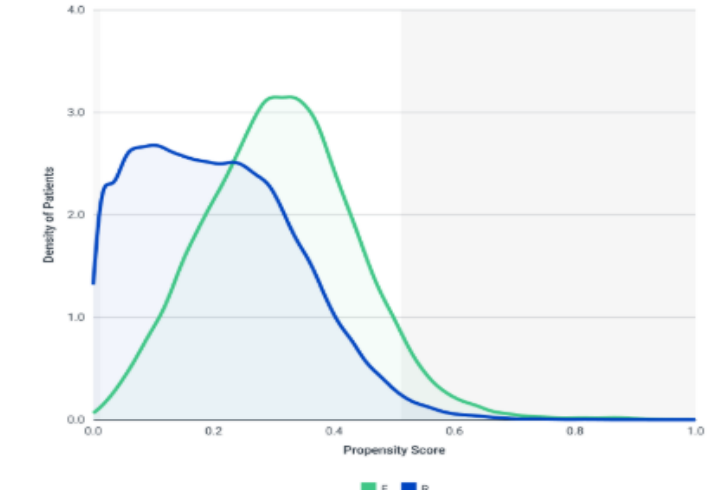
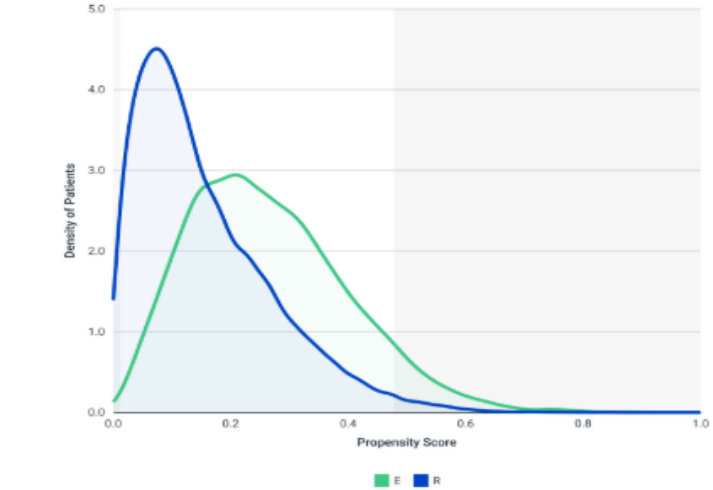


Figure 63: Pre-matching propensity score overlap

Figure 63: Pre-matching propensity score overlap

The c-statistics for the propensity score model, pre-matching was 0.744. The post-matching c-statistic was 0.538.

The c-statistics for the propensity score model, pre-matching was 0.722. The post-matching c-statistic was 0.528.

AFTER PS MATCHING

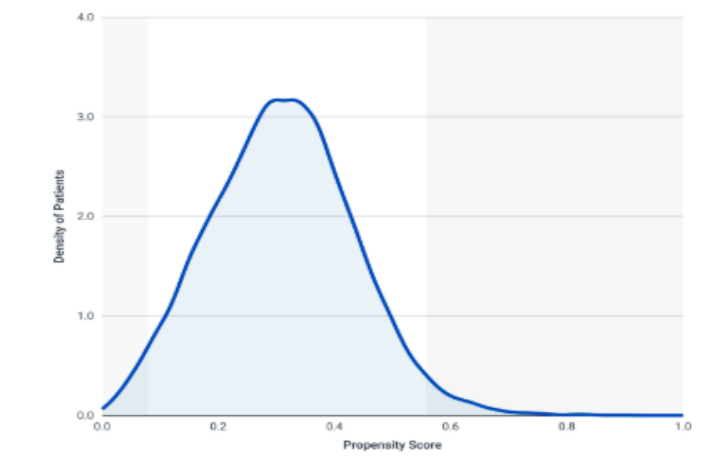
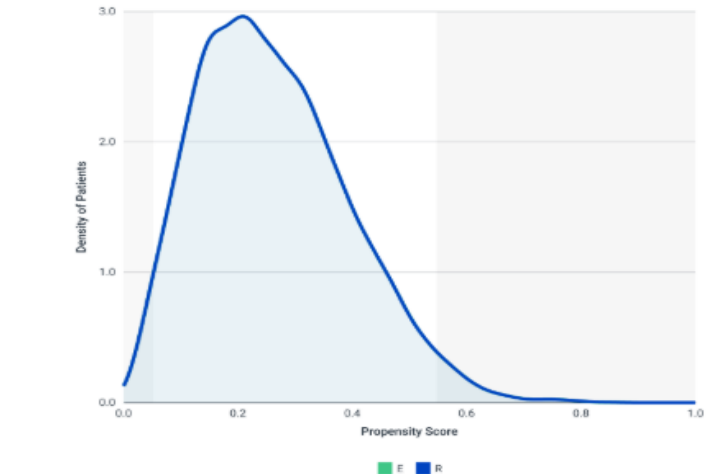


Figure 64: Post-matching propensity score overlap

Figure 64: Post-matching propensity score overlap

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Variable	Unmatched								
	Optum			Truven			POOLED		
	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.
Number of patients	34,251	7,078		32,565	8,264		66,816	15,342	
Age									
...mean (sd)	70.43 (10.74)	67.99 (10.81)	0.23	66.08 (12.03)	62.10 (10.28)	0.36	68.31 (11.39)	64.82 (10.53)	0.32
...median [IQR]	71.00 [64.00, 79.00]	69.00 [61.00, 76.00]	0.19	64.00 [59.00, 74.00]	62.00 [56.00, 67.00]	0.18	67.59 (11.39)	65.23 (10.53)	0.22
Age categories									
...18 - 54; n (%)	2,810 (8.2%)	821 (11.6%)	-0.11	4,940 (15.2%)	1,688 (20.4%)	-0.14	7,750 (11.6%)	2,509 (16.4%)	-0.14
...55 - 64; n (%)	6,438 (18.8%)	1,599 (22.6%)	-0.09	12,321 (37.8%)	4,014 (48.6%)	-0.22	18,759 (28.1%)	5,613 (36.6%)	-0.18
...65 - 74; n (%)	12,095 (35.3%)	2,625 (37.1%)	-0.04	7,185 (22.1%)	1,526 (18.5%)	0.09	19,280 (28.9%)	4,151 (27.1%)	0.04
...≥ 75; n (%)	12,908 (37.7%)	2,033 (28.7%)	0.19	8,119 (24.9%)	1,036 (12.5%)	0.32	21,027 (31.5%)	3,069 (20.0%)	0.27
Gender									
...Males; n (%)	21,162 (61.8%)	4,536 (64.1%)	-0.05	21,484 (66.0%)	5,919 (71.6%)	-0.12	42,646 (63.8%)	10,455 (68.1%)	-0.09
...Females; n (%)	13,089 (38.2%)	2,542 (35.9%)	0.05	11,081 (34.0%)	2,345 (28.4%)	0.12	24,170 (36.2%)	4,887 (31.9%)	0.09
Region									
...Northeast; n (%)	4,152 (12.1%)	804 (11.4%)	0.02	6,331 (19.4%)	1,562 (18.9%)	0.01	10,483 (15.7%)	2,366 (15.4%)	0.01
...South; n (%)	14,216 (41.5%)	3,335 (47.1%)	-0.11	9,450 (29.0%)	2,199 (26.6%)	0.05	23,666 (35.4%)	5,534 (36.1%)	-0.01
...Midwest; n (%)	8,706 (25.4%)	1,626 (23.0%)	0.06	11,688 (35.9%)	3,597 (43.5%)	-0.16	20,394 (30.5%)	5,223 (34.0%)	-0.07
...West; n (%)	7,177 (21.0%)	1,313 (18.6%)	0.06	4,769 (14.6%)	868 (10.5%)	0.12	11,946 (17.9%)	2,181 (14.2%)	0.10
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	327 (1.0%)	38 (0.5%)	0.06	327 (0.5%)	38 (0.2%)	0.05
CV Covariates									
Ischemic heart disease; n (%)	34,251 (100.0%)	7,078 (100.0%)	#DIV/0!	32,565 (100.0%)	8,264 (100.0%)	#DIV/0!	66,816 (100.0%)	15,342 (100.0%)	#DIV/0!
Acute MI; n (%)	31,334 (91.5%)	6,496 (91.8%)	-0.01	31,063 (95.4%)	7,831 (94.8%)	0.03	62397 (93.4%)	14327 (93.4%)	0.00
ACS/unstable angina; n (%)	14,701 (42.9%)	2,968 (41.9%)	0.02	11,618 (35.7%)	2,960 (35.8%)	0.00	26319 (39.4%)	5928 (38.6%)	0.02
Old MI; n (%)	5,865 (17.1%)	1,180 (16.7%)	0.01	3,170 (9.7%)	720 (8.7%)	0.03	9035 (13.5%)	1900 (12.4%)	0.03
Stable angina; n (%)	8,209 (24.0%)	1,781 (25.2%)	-0.03	4,741 (14.6%)	1,380 (16.7%)	-0.06	12,950 (19.4%)	3,161 (20.6%)	-0.03
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	32,438 (94.7%)	6,799 (96.1%)	-0.07	29,092 (89.3%)	7,630 (92.3%)	-0.10	61,530 (92.1%)	14,429 (94.0%)	-0.07
Other atherosclerosis with ICD10 ; n (%)	634 (1.9%)	84 (1.2%)	0.06	632 (1.9%)	89 (1.1%)	0.07	1266 (1.9%)	173 (1.1%)	0.07
Previous cardiac procedure (CABG or PTCA or Stent) ; n (%)	25,241 (73.7%)	6,564 (92.7%)	-0.53	24,229 (74.4%)	7,510 (90.9%)	-0.45	49470 (74.0%)	14074 (91.7%)	-0.48
History of CABG or PTCA; n (%)	12,033 (35.1%)	2,459 (34.7%)	0.01	5,974 (18.3%)	1,489 (18.0%)	0.01	18,007 (27.0%)	3,948 (25.7%)	0.03
Any stroke; n (%)	4,738 (13.8%)	622 (8.8%)	0.16	3,006 (9.2%)	433 (5.2%)	0.16	7,744 (11.6%)	1,055 (6.9%)	0.16
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	4,698 (13.7%)	619 (8.7%)	0.16	2,999 (9.2%)	433 (5.2%)	0.16	7,697 (11.5%)	1,052 (6.9%)	0.16
Hemorrhagic stroke; n (%)	77 (0.2%)	8 (0.1%)	0.03	9 (0.0%)	0 (0.0%)	#DIV/0!	86 (0.1%)	8 (0.1%)	0.00
TIA; n (%)	829 (2.4%)	128 (1.8%)	0.04	595 (1.8%)	81 (1.0%)	0.07	1424 (2.1%)	209 (1.4%)	0.05
Other cerebrovascular disease; n (%)	1,088 (3.2%)	153 (2.2%)	0.06	565 (1.7%)	77 (0.9%)	0.07	1653 (2.5%)	230 (1.5%)	0.07
Late effects of cerebrovascular disease; n (%)	888 (2.6%)	139 (2.0%)	0.04	337 (1.0%)	54 (0.7%)	0.03	1225 (1.8%)	193 (1.3%)	0.04
Cerebrovascular procedure; n (%)	71 (0.2%)	8 (0.1%)	0.03	49 (0.2%)	4 (0.0%)	0.06	120 (0.2%)	12 (0.1%)	0.03
Heart failure (CHF); n (%)	10,773 (31.5%)	1,796 (25.4%)	0.14	7,073 (21.7%)	1,226 (14.8%)	0.18	17,846 (26.7%)	3,022 (19.7%)	0.17
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	4,708 (13.7%)	884 (12.5%)	0.04	2,400 (7.4%)	428 (5.2%)	0.09	7,108 (10.6%)	1,312 (8.6%)	0.07
Atrial fibrillation; n (%)	6,613 (19.3%)	833 (11.8%)	0.21	4,094 (12.6%)	587 (7.1%)	0.19	10,707 (16.0%)	1,420 (9.3%)	0.20
Other cardiac dysrhythmia; n (%)	13,828 (40.4%)	2,626 (37.1%)	0.07	9,711 (29.8%)	2,478 (30.0%)	0.00	23,539 (35.2%)	5,104 (33.3%)	0.04

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Cardiac conduction disorders; n (%)	5,955 (17.4%)	1,074 (15.2%)	0.06	3,681 (11.3%)	813 (9.8%)	0.05	9636 (14.4%)	1887 (12.3%)	0.06
Other CVD; n (%)	14,535 (42.4%)	2,682 (37.9%)	0.09	9,954 (30.6%)	2,194 (26.5%)	0.09	24,489 (36.7%)	4,876 (31.8%)	0.10
Diabetes-related complications									
Diabetic retinopathy; n (%)	1,230 (3.6%)	273 (3.9%)	-0.02	633 (1.9%)	154 (1.9%)	0.00	1,863 (2.8%)	0,427 (2.8%)	0.00
Diabetes with other ophthalmic manifestations; n (%)	105 (0.3%)	36 (0.5%)	-0.03	422 (1.3%)	75 (0.9%)	0.04	0,527 (0.8%)	0,111 (0.7%)	0.01
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	147 (0.4%)	17 (0.2%)	0.04	74 (0.2%)	24 (0.3%)	-0.02	221 (0.3%)	41 (0.3%)	0.00
Retinal laser coagulation therapy; n (%)	127 (0.4%)	31 (0.4%)	0.00	113 (0.3%)	36 (0.4%)	-0.02	240 (0.4%)	67 (0.4%)	0.00
Occurrence of Diabetic Neuropathy ; n (%)	3,634 (10.6%)	902 (12.7%)	-0.07	1,671 (5.1%)	430 (5.2%)	0.00	5,305 (7.9%)	1,332 (8.7%)	-0.03
Occurrence of diabetic nephropathy with ICD10 ; n (%)	3,723 (10.9%)	859 (12.1%)	-0.04	1,057 (3.2%)	259 (3.1%)	0.01	4,780 (7.2%)	1,118 (7.3%)	0.00
Hypoglycemia ; n (%)	529 (1.5%)	40 (0.6%)	0.09	598 (1.8%)	96 (1.2%)	0.05	1,127 (1.7%)	0,136 (0.9%)	0.07
Hyperglycemia; n (%)	2,999 (8.8%)	639 (9.0%)	-0.01	1,715 (5.3%)	497 (6.0%)	-0.03	4,714 (7.1%)	1,136 (7.4%)	-0.01
Disorders of fluid electrolyte and acid-base balance; n (%)	7,300 (21.3%)	1,404 (19.8%)	0.04	3,644 (11.2%)	793 (9.6%)	0.05	10,944 (16.4%)	2,197 (14.3%)	0.06
Diabetic ketoacidosis; n (%)	217 (0.6%)	40 (0.6%)	0.00	189 (0.6%)	49 (0.6%)	0.00	406 (0.6%)	89 (0.6%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	154 (0.4%)	34 (0.5%)	-0.01	56 (0.2%)	13 (0.2%)	0.00	210 (0.3%)	47 (0.3%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	1,964 (5.7%)	470 (6.6%)	-0.04	652 (2.0%)	145 (1.8%)	0.01	2,616 (3.9%)	0,615 (4.0%)	-0.01
Diabetic Foot; n (%)	655 (1.9%)	104 (1.5%)	0.03	412 (1.3%)	74 (0.9%)	0.04	1067 (1.6%)	178 (1.2%)	0.03
Gangrene ; n (%)	80 (0.2%)	9 (0.1%)	0.03	38 (0.1%)	4 (0.0%)	0.04	118 (0.2%)	13 (0.1%)	0.03
Lower extremity amputation; n (%)	258 (0.8%)	45 (0.6%)	0.02	70 (0.2%)	17 (0.2%)	0.00	328 (0.5%)	62 (0.4%)	0.01
Osteomyelitis; n (%)	144 (0.4%)	30 (0.4%)	0.00	88 (0.3%)	23 (0.3%)	0.00	232 (0.3%)	53 (0.3%)	0.00
Skin infections ; n (%)	1,789 (5.2%)	325 (4.6%)	0.03	1,272 (3.9%)	294 (3.6%)	0.02	3,061 (4.6%)	0,619 (4.0%)	0.03
Erectile dysfunction; n (%)	895 (2.6%)	230 (3.2%)	-0.04	634 (1.9%)	197 (2.4%)	-0.03	1,529 (2.3%)	0,427 (2.8%)	-0.03
Diabetes with unspecified complication; n (%)	1,412 (4.1%)	409 (5.8%)	-0.08	758 (2.3%)	278 (3.4%)	-0.07	2,170 (3.2%)	0,687 (4.5%)	-0.07
Diabetes mellitus without mention of complications; n (%)	15,987 (46.7%)	3,767 (53.2%)	-0.13	13,028 (40.0%)	3,410 (41.3%)	-0.03	29,015 (43.4%)	7,177 (46.8%)	-0.07
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	29,781 (86.9%)	6,140 (86.7%)	0.01	24,582 (75.5%)	6,362 (77.0%)	-0.04	54,363 (81.4%)	12,502 (81.5%)	0.00
Hyperlipidemia ; n (%)	28,216 (82.4%)	5,950 (84.1%)	-0.05	21,320 (65.5%)	5,887 (71.2%)	-0.12	49,536 (74.1%)	11,837 (77.2%)	-0.07
Edema; n (%)	2,760 (8.1%)	463 (6.5%)	0.06	1,232 (3.8%)	240 (2.9%)	0.05	3,992 (6.0%)	0,703 (4.6%)	0.06
Renal Dysfunction (non-diabetic) ; n (%)	10,997 (32.1%)	2,153 (30.4%)	0.04	5,565 (17.1%)	1,067 (12.9%)	0.12	16,562 (24.8%)	3,220 (21.0%)	0.09
Occurrence of acute renal disease ; n (%)	5,186 (15.1%)	967 (13.7%)	0.04	2,495 (7.7%)	464 (5.6%)	0.08	7681 (11.5%)	1431 (9.3%)	0.07
Occurrence of chronic renal insufficiency; n (%)	8,114 (23.7%)	1,581 (22.3%)	0.03	3,144 (9.7%)	565 (6.8%)	0.11	11,258 (16.8%)	2,146 (14.0%)	0.08
Chronic kidney disease ; n (%)	7,938 (23.2%)	1,541 (21.8%)	0.03	3,053 (9.4%)	537 (6.5%)	0.11	10,991 (16.4%)	2,078 (13.5%)	0.08
CKD Stage 3-4; n (%)	5,647 (16.5%)	1,103 (15.6%)	0.02	1,963 (6.0%)	358 (4.3%)	0.08	7,610 (11.4%)	1,461 (9.5%)	0.06
Occurrence of hypertensive nephropathy; n (%)	6,374 (18.6%)	1,237 (17.5%)	0.03	2,370 (7.3%)	390 (4.7%)	0.11	8744 (13.1%)	1627 (10.6%)	0.08
Occurrence of miscellaneous renal insufficiency ; n (%)	3,321 (9.7%)	626 (8.8%)	0.03	1,555 (4.8%)	344 (4.2%)	0.03	4,876 (7.3%)	0,970 (6.3%)	0.04
Glaucoma or cataracts ; n (%)	5,574 (16.3%)	1,117 (15.8%)	0.01	4,135 (12.7%)	898 (10.9%)	0.06	9,709 (14.5%)	2,015 (13.1%)	0.04
Cellulitis or abscess of toe; n (%)	474 (1.4%)	87 (1.2%)	0.02	184 (0.6%)	56 (0.7%)	-0.01	658 (1.0%)	143 (0.9%)	0.01

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Foot ulcer; n (%)	661 (1.9%)	107 (1.5%)	0.03	415 (1.3%)	72 (0.9%)	0.04	1076 (1.6%)	179 (1.2%)	0.03
Bladder stones; n (%)	78 (0.2%)	9 (0.1%)	0.03	30 (0.1%)	9 (0.1%)	0.00	108 (0.2%)	18 (0.1%)	0.03
Kidney stones; n (%)	961 (2.8%)	220 (3.1%)	-0.02	521 (1.6%)	148 (1.8%)	-0.02	1,482 (2.2%)	0,368 (2.4%)	-0.01
Urinary tract infections (UTIs); n (%)	3,662 (10.7%)	627 (8.9%)	0.06	1,767 (5.4%)	308 (3.7%)	0.08	5,429 (8.1%)	0,935 (6.1%)	0.08
Dipstick urinalysis; n (%)	9,527 (27.8%)	1,976 (27.9%)	0.00	6,727 (20.7%)	1,658 (20.1%)	0.01	16,254 (24.3%)	3,634 (23.7%)	0.01
Non-dipstick urinalysis; n (%)	5,596 (16.3%)	1,400 (19.8%)	-0.09	3,038 (9.3%)	864 (10.5%)	-0.04	8,634 (12.9%)	2,264 (14.8%)	-0.06
Urine function test; n (%)	867 (2.5%)	162 (2.3%)	0.01	619 (1.9%)	156 (1.9%)	0.00	1,486 (2.2%)	0,318 (2.1%)	0.01
Cytology; n (%)	410 (1.2%)	84 (1.2%)	0.00	179 (0.5%)	37 (0.4%)	0.01	589 (0.9%)	121 (0.8%)	0.01
Cystos; n (%)	597 (1.7%)	106 (1.5%)	0.02	233 (0.7%)	43 (0.5%)	0.03	830 (1.2%)	149 (1.0%)	0.02
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0,000 (0.0%)	#DIV/0!
Osteoarthritis; n (%)	7,052 (20.6%)	1,438 (20.3%)	0.01	4,240 (13.0%)	988 (12.0%)	0.03	11,292 (16.9%)	2,426 (15.8%)	0.03
Other arthritis, arthropathies and musculoskeletal pain; n (%)	13,667 (39.9%)	2,723 (38.5%)	0.03	10,227 (31.4%)	2,471 (29.9%)	0.03	23,894 (35.8%)	5,194 (33.9%)	0.04
Dorsopathies; n (%)	9,026 (26.4%)	1,846 (26.1%)	0.01	6,582 (20.2%)	1,668 (20.2%)	0.00	15,608 (23.4%)	3,514 (22.9%)	0.01
Fractures; n (%)	1,178 (3.4%)	202 (2.9%)	0.03	737 (2.3%)	153 (1.9%)	0.03	1,915 (2.9%)	0,355 (2.3%)	0.04
Falls; n (%)	1,563 (4.6%)	267 (3.8%)	0.04	370 (1.1%)	70 (0.8%)	0.03	1933 (2.9%)	337 (2.2%)	0.04
Osteoporosis; n (%)	2,018 (5.9%)	328 (4.6%)	0.06	1,062 (3.3%)	164 (2.0%)	0.08	3,080 (4.6%)	0,492 (3.2%)	0.07
Hyperthyroidism; n (%)	239 (0.7%)	47 (0.7%)	0.00	134 (0.4%)	29 (0.4%)	0.00	373 (0.6%)	76 (0.5%)	0.01
Hypothyroidism ; n (%)	5,722 (16.7%)	1,155 (16.3%)	0.01	3,460 (10.6%)	809 (9.8%)	0.03	9,182 (13.7%)	1,964 (12.8%)	0.03
Other disorders of thyroid gland ; n (%)	1,009 (2.9%)	246 (3.5%)	-0.03	684 (2.1%)	176 (2.1%)	0.00	1,693 (2.5%)	0,422 (2.8%)	-0.02
Depression; n (%)	4,071 (11.9%)	818 (11.6%)	0.01	2,357 (7.2%)	499 (6.0%)	0.05	6,428 (9.6%)	1,317 (8.6%)	0.03
Anxiety; n (%)	4,488 (13.1%)	986 (13.9%)	-0.02	2,477 (7.6%)	682 (8.3%)	-0.03	6,965 (10.4%)	1,668 (10.9%)	-0.02
SleepDisorder; n (%)	2,233 (6.5%)	322 (4.5%)	0.09	2,524 (7.8%)	461 (5.6%)	0.09	4,757 (7.1%)	0,783 (5.1%)	0.08
Dementia; n (%)	2,499 (7.3%)	310 (4.4%)	0.12	1,211 (3.7%)	120 (1.5%)	0.14	3710 (5.6%)	430 (2.8%)	0.14
Delirium; n (%)	1,054 (3.1%)	159 (2.2%)	0.06	505 (1.6%)	73 (0.9%)	0.06	1559 (2.3%)	232 (1.5%)	0.06
Psychosis; n (%)	499 (1.5%)	64 (0.9%)	0.06	252 (0.8%)	37 (0.4%)	0.05	751 (1.1%)	101 (0.7%)	0.04
Obesity; n (%)	7,787 (22.7%)	1,982 (28.0%)	-0.12	5,186 (15.9%)	1,595 (19.3%)	-0.09	12,973 (19.4%)	3,577 (23.3%)	-0.10
Overweight; n (%)	1,859 (5.4%)	522 (7.4%)	-0.08	666 (2.0%)	250 (3.0%)	-0.06	2,525 (3.8%)	0,772 (5.0%)	-0.06
Smoking; n (%)	14,843 (43.3%)	3,268 (46.2%)	-0.06	8,437 (25.9%)	2,368 (28.7%)	-0.06	23,280 (34.8%)	5,636 (36.7%)	-0.04
Alcohol abuse or dependence; n (%)	838 (2.4%)	166 (2.3%)	0.01	556 (1.7%)	122 (1.5%)	0.02	1394 (2.1%)	288 (1.9%)	0.01
Drug abuse or dependence; n (%)	883 (2.6%)	198 (2.8%)	-0.01	380 (1.2%)	105 (1.3%)	-0.01	1263 (1.9%)	303 (2.0%)	-0.01
COPD; n (%)	7,224 (21.1%)	1,272 (18.0%)	0.08	4,050 (12.4%)	686 (8.3%)	0.13	11,274 (16.9%)	1,958 (12.8%)	0.12
Asthma; n (%)	2,569 (7.5%)	519 (7.3%)	0.01	1,779 (5.5%)	406 (4.9%)	0.03	4,348 (6.5%)	0,925 (6.0%)	0.02
Obstructive sleep apnea; n (%)	3,355 (9.8%)	841 (11.9%)	-0.07	2,502 (7.7%)	709 (8.6%)	-0.03	5,857 (8.8%)	1,550 (10.1%)	-0.04
Pneumonia; n (%)	2,786 (8.1%)	472 (6.7%)	0.05	1,673 (5.1%)	234 (2.8%)	0.12	4,459 (6.7%)	0,706 (4.6%)	0.09
Imaging; n (%)	835 (2.4%)	216 (3.1%)	-0.04	4,135 (12.7%)	113 (1.4%)	0.45	1227 (1.8%)	329 (2.1%)	-0.02
Other Medications									
Use of ACE inhibitors; n (%)	18,168 (53.0%)	3,711 (52.4%)	0.01	18,195 (55.9%)	4,684 (56.7%)	-0.02	36,363 (54.4%)	8,395 (54.7%)	-0.01
Use of ARBs; n (%)	7,250 (21.2%)	1,772 (25.0%)	-0.09	6,486 (19.9%)	1,768 (21.4%)	-0.04	13,736 (20.6%)	3,540 (23.1%)	-0.06
Use of Loop Diuretics - ; n (%)	7,459 (21.8%)	1,065 (15.0%)	0.18	5,065 (15.6%)	615 (7.4%)	0.26	12,524 (18.7%)	1,680 (11.0%)	0.22
Use of other diuretics- ; n (%)	1,797 (5.2%)	346 (4.9%)	0.01	1,516 (4.7%)	346 (4.2%)	0.02	3,313 (5.0%)	0,692 (4.5%)	0.02
Use of nitrates- ; n (%)	15,391 (44.9%)	3,062 (43.3%)	0.03	15,249 (46.8%)	3,618 (43.8%)	0.06	30,640 (45.9%)	6,680 (43.5%)	0.05
Use of other hypertension drugs; n (%)	3,062 (8.9%)	529 (7.5%)	0.05	2,130 (6.5%)	372 (4.5%)	0.09	5,192 (7.8%)	0,901 (5.9%)	0.08
Use of digoxin- ; n (%)	772 (2.3%)	72 (1.0%)	0.10	703 (2.2%)	64 (0.8%)	0.12	1475 (2.2%)	136 (0.9%)	0.11
Use of Anti-arrhythmics; n (%)	1,992 (5.8%)	204 (2.9%)	0.14	1,521 (4.7%)	157 (1.9%)	0.16	3513 (5.3%)	361 (2.4%)	0.15
Use of COPD/asthma meds- ; n (%)	5,251 (15.3%)	1,080 (15.3%)	0.00	4,557 (14.0%)	990 (12.0%)	0.06	9,808 (14.7%)	2,070 (13.5%)	0.03
Use of statins; n (%)	30,368 (88.7%)	6,399 (90.4%)	-0.06	29,034 (89.2%)	7,587 (91.8%)	-0.09	59,402 (88.9%)	13,986 (91.2%)	-0.08

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Use of other lipid-lowering drugs; n (%)	2,561 (7.5%)	545 (7.7%)	-0.01	2,974 (9.1%)	754 (9.1%)	0.00	5,535 (8.3%)	1,299 (8.5%)	-0.01
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	3,350 (9.8%)	353 (5.0%)	0.18	2,682 (8.2%)	321 (3.9%)	0.18	6,032 (9.0%)	0,674 (4.4%)	0.18
Use of heparin and other low-molecular weight heparins; n (%)	384 (1.1%)	41 (0.6%)	0.05	3 (0.0%)	0 (0.0%)	#DIV/0!	387 (0.6%)	41 (0.3%)	0.04
Use of NSAIDs; n (%)	4,499 (13.1%)	1,078 (15.2%)	-0.06	4,253 (13.1%)	1,298 (15.7%)	-0.07	8,752 (13.1%)	2,376 (15.5%)	-0.07
Use of oral corticosteroids; n (%)	6,426 (18.8%)	1,272 (18.0%)	0.02	5,175 (15.9%)	1,257 (15.2%)	0.02	11,601 (17.4%)	2,529 (16.5%)	0.02
Use of bisphosphonate (); n (%)	783 (2.3%)	114 (1.6%)	0.05	554 (1.7%)	67 (0.8%)	0.08	1337 (2.0%)	181 (1.2%)	0.06
Use of opioids-; n (%)	10,025 (29.3%)	1,741 (24.6%)	0.11	8,554 (26.3%)	1,758 (21.3%)	0.12	18,579 (27.8%)	3,499 (22.8%)	0.12
Use of antidepressants; n (%)	6,765 (19.8%)	1,410 (19.9%)	0.00	5,528 (17.0%)	1,302 (15.8%)	0.03	12,293 (18.4%)	2,712 (17.7%)	0.02
Use of antipsychotics; n (%)	665 (1.9%)	145 (2.0%)	-0.01	418 (1.3%)	74 (0.9%)	0.04	1,083 (1.6%)	0,219 (1.4%)	0.02
Use of anticonvulsants; n (%)	4,151 (12.1%)	968 (13.7%)	-0.05	2,669 (8.2%)	652 (7.9%)	0.01	6,820 (10.2%)	1,620 (10.6%)	-0.01
Use of lithium-; n (%)	41 (0.1%)	11 (0.2%)	-0.03	35 (0.1%)	6 (0.1%)	0.00	76 (0.1%)	17 (0.1%)	0.00
Use of Benzos-; n (%)	3,677 (10.7%)	793 (11.2%)	-0.02	3,590 (11.0%)	852 (10.3%)	0.02	7,267 (10.9%)	1,645 (10.7%)	0.01
Use of anxiolytics/hypnotics-; n (%)	1,644 (4.8%)	316 (4.5%)	0.01	1,835 (5.6%)	441 (5.3%)	0.01	3,479 (5.2%)	0,757 (4.9%)	0.01
Use of dementia meds-; n (%)	924 (2.7%)	123 (1.7%)	0.07	648 (2.0%)	61 (0.7%)	0.11	1572 (2.4%)	184 (1.2%)	0.09
Use of antiparkinsonian meds-; n (%)	805 (2.4%)	159 (2.2%)	0.01	576 (1.8%)	117 (1.4%)	0.03	1,381 (2.1%)	0,276 (1.8%)	0.02
Entresto (sacubitril/valsartan); n (%)	58 (0.2%)	16 (0.2%)	0.00	9 (0.0%)	3 (0.0%)	#DIV/0!	67 (0.1%)	19 (0.1%)	0.00
Labs							0	0	
Lab values- HbA1c (%) ; n (%)	5,587 (16.3%)	1,481 (20.9%)	-0.12	570 (1.8%)	128 (1.5%)	0.02	6,157 (9.2%)	1,609 (10.5%)	-0.04
Lab values- HbA1c (%) (within 3 months); n (%)	3,598 (10.5%)	955 (13.5%)	-0.09	395 (1.2%)	93 (1.1%)	0.01	3,993 (6.0%)	1,048 (6.8%)	-0.03
Lab values- HbA1c (%) (within 6 months); n (%)	5,587 (16.3%)	1,481 (20.9%)	-0.12	570 (1.8%)	128 (1.5%)	0.02	6,157 (9.2%)	1,609 (10.5%)	-0.04
Lab values- BNP; n (%)	376 (1.1%)	75 (1.1%)	0.00	44 (0.1%)	2 (0.0%)	0.04	420 (0.6%)	77 (0.5%)	0.01
Lab values- BNP (within 3 months); n (%)	290 (0.8%)	54 (0.8%)	0.00	39 (0.1%)	1 (0.0%)	0.04	329 (0.5%)	55 (0.4%)	0.01
Lab values- BNP (within 6 months); n (%)	376 (1.1%)	75 (1.1%)	0.00	44 (0.1%)	2 (0.0%)	0.04	420 (0.6%)	77 (0.5%)	0.01
Lab values- BUN (mg/dl); n (%)	8,281 (24.2%)	2,014 (28.5%)	-0.10	452 (1.4%)	141 (1.7%)	-0.02	8,733 (13.1%)	2,155 (14.0%)	-0.03
Lab values- BUN (mg/dl) (within 3 months); n (%)	5,410 (15.8%)	1,335 (18.9%)	-0.08	310 (1.0%)	88 (1.1%)	-0.01	5,720 (8.6%)	1,423 (9.3%)	-0.02
Lab values- BUN (mg/dl) (within 6 months); n (%)	8,281 (24.2%)	2,014 (28.5%)	-0.10	452 (1.4%)	141 (1.7%)	-0.02	8,733 (13.1%)	2,155 (14.0%)	-0.03
Lab values- Creatinine (mg/dl) ; n (%)	8,490 (24.8%)	2,074 (29.3%)	-0.10	475 (1.5%)	152 (1.8%)	-0.02	8,965 (13.4%)	2,226 (14.5%)	-0.03
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	5,559 (16.2%)	1,382 (19.5%)	-0.09	322 (1.0%)	98 (1.2%)	-0.02	5,881 (8.8%)	1,480 (9.6%)	-0.03
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	8,490 (24.8%)	2,074 (29.3%)	-0.10	475 (1.5%)	152 (1.8%)	-0.02	8,965 (13.4%)	2,226 (14.5%)	-0.03
Lab values- HDL level (mg/dl); n (%)	6,291 (18.4%)	1,583 (22.4%)	-0.10	482 (1.5%)	121 (1.5%)	0.00	6,773 (10.1%)	1,704 (11.1%)	-0.03
Lab values- HDL level (mg/dl) (within 3 months); n (%)	3,750 (10.9%)	955 (13.5%)	-0.08	304 (0.9%)	71 (0.9%)	0.00	4,054 (6.1%)	1,026 (6.7%)	-0.02
Lab values- HDL level (mg/dl) (within 6 months); n (%)	6,291 (18.4%)	1,583 (22.4%)	-0.10	482 (1.5%)	121 (1.5%)	0.00	6,773 (10.1%)	1,704 (11.1%)	-0.03
Lab values- LDL level (mg/dl) ; n (%)	6,448 (18.8%)	1,656 (23.4%)	-0.11	546 (1.7%)	129 (1.6%)	0.01	6,994 (10.5%)	1,785 (11.6%)	-0.04
Lab values- LDL level (mg/dl) (within 3 months); n (%)	3,851 (11.2%)	1,012 (14.3%)	-0.09	367 (1.1%)	78 (0.9%)	0.02	4,218 (6.3%)	1,090 (7.1%)	-0.03
Lab values- LDL level (mg/dl) (within 6 months); n (%)	6,448 (18.8%)	1,656 (23.4%)	-0.11	546 (1.7%)	129 (1.6%)	0.01	6,994 (10.5%)	1,785 (11.6%)	-0.04
Lab values- NT-proBNP; n (%)	61 (0.2%)	11 (0.2%)	0.00	1 (0.0%)	1 (0.0%)	#DIV/0!	62 (0.1%)	12 (0.1%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Lab values- NT-proBNP (within 3 months); n (%)	47 (0.1%)	7 (0.1%)	0.00	1 (0.0%)	1 (0.0%)	#DIV/0!	48 (0.1%)	8 (0.1%)	0.00
Lab values- NT-proBNP (within 6 months); n (%)	61 (0.2%)	11 (0.2%)	0.00	1 (0.0%)	1 (0.0%)	#DIV/0!	62 (0.1%)	12 (0.1%)	0.00
Lab values- Total cholesterol (mg/dl) ; n (%)	6,353 (18.5%)	1,612 (22.8%)	-0.11	471 (1.4%)	123 (1.5%)	-0.01	6,824 (10.2%)	1,735 (11.3%)	-0.04
Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (%)	3,786 (11.1%)	970 (13.7%)	-0.08	298 (0.9%)	71 (0.9%)	0.00	4,084 (6.1%)	1,041 (6.8%)	-0.03
Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%)	6,353 (18.5%)	1,612 (22.8%)	-0.11	471 (1.4%)	123 (1.5%)	-0.01	6,824 (10.2%)	1,735 (11.3%)	-0.04
Lab values- Triglyceride level (mg/dl); n (%)	6,221 (18.2%)	1,597 (22.6%)	-0.11	472 (1.4%)	119 (1.4%)	0.00	6,693 (10.0%)	1,716 (11.2%)	-0.04
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	3,695 (10.8%)	963 (13.6%)	-0.09	296 (0.9%)	70 (0.8%)	0.01	3,991 (6.0%)	1,033 (6.7%)	-0.03
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	6,221 (18.2%)	1,597 (22.6%)	-0.11	472 (1.4%)	119 (1.4%)	0.00	6,693 (10.0%)	1,716 (11.2%)	-0.04
Lab result number- HbA1c (%) mean (only 2 to 20 included)	5,556	1,478		464	125		0	0	
...mean (sd)	7.20 (1.75)	7.29 (1.78)	-0.05	8.06 (1.91)	7.73 (1.79)	0.18	7.62 (1.83)	7.53 (1.79)	0.05
...median [IQR]	6.70 [6.00, 7.90]	6.80 [6.00, 8.08]	-0.06	7.55 [6.60, 9.20]	7.30 [6.30, 9.00]	0.14	7.11 (1.83)	7.07 (1.79)	0.02
...Missing; n (%)	28,695 (83.8%)	5,600 (79.1%)	0.12	32,101 (98.6%)	8,139 (98.5%)	0.01	60,796 (91.0%)	13,739 (89.6%)	0.05
Lab result number- BNP mean	376	75		44	2		0	0	
...mean (sd)	527.10 (1,591.70)	345.44 (674.53)	0.15	900.99 (2,781.11)	334.50 (0.71)	0.29	709.33 (2251.31)	339.55 (458.16)	0.23
...median [IQR]	163.50 [67.92, 456.20]	99.00 [44.50, 280.00]	0.05	180.00 [51.75, 426.75]	334.50 [334.00, 335.00]	-0.08	171.54 (2251.31)	225.85 (458.16)	-0.03
...Missing; n (%)	33,875 (98.9%)	7,003 (98.9%)	0.00	32,521 (99.9%)	8,262 (100.0%)	-0.04	66,396 (99.4%)	15,265 (99.5%)	-0.01
Lab result number- BUN (mg/dl) mean	8,281	2,014		452	141		0	0	
...mean (sd)	19.75 (9.07)	18.87 (7.63)	0.10	571.73 (8,364.27)	2,768.72 (19,247.11)	-0.15	288.78 (5839.34)	1500.08 (14126.08)	-0.11
...median [IQR]	18.00 [14.00, 23.00]	17.00 [14.00, 22.00]	0.12	17.00 [14.00, 21.46]	17.00 [13.50, 21.00]	0.00	17.51 (5839.34)	17.00 (14126.08)	0.00
...Missing; n (%)	25,970 (75.8%)	5,064 (71.5%)	0.10	32,113 (98.6%)	8,123 (98.3%)	0.02	58,083 (86.9%)	13,187 (86.0%)	0.03
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	8,378	2,055		426	124		0	0	
...mean (sd)	1.11 (0.46)	1.08 (0.40)	0.07	1.05 (0.59)	1.00 (0.23)	0.11	1.08 (0.53)	1.04 (0.32)	0.09
...median [IQR]	1.01 [0.85, 1.24]	1.00 [0.84, 1.21]	0.02	0.98 [0.83, 1.12]	1.00 [0.88, 1.08]	-0.04	1.00 (0.53)	1.00 (0.32)	0.00
...Missing; n (%)	25,873 (75.5%)	5,023 (71.0%)	0.10	32,139 (98.7%)	8,140 (98.5%)	0.02	58,012 (86.8%)	13,163 (85.8%)	0.03
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	6,291	1,583		480	121		0	0	
...mean (sd)	47.14 (15.16)	46.42 (13.96)	0.05	41.22 (13.28)	42.43 (12.34)	-0.09	44.25 (14.27)	44.27 (13.11)	0.00
...median [IQR]	45.00 [37.00, 55.00]	44.00 [37.00, 54.00]	0.07	40.00 [34.00, 49.00]	40.00 [35.00, 50.00]	0.00	42.56 (14.27)	41.85 (13.11)	0.05
...Missing; n (%)	27,960 (81.6%)	5,495 (77.6%)	0.10	32,085 (98.5%)	8,143 (98.5%)	0.00	60,045 (89.9%)	13,638 (88.9%)	0.03
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	6,290	1,620		465	114		0	0	
...mean (sd)	99.66 (43.64)	103.21 (43.70)	-0.08	95.58 (49.98)	97.40 (47.25)	-0.04	97.67 (46.84)	100.08 (45.65)	-0.05
...median [IQR]	97.00 [72.00, 126.00]	100.00 [75.00, 130.00]	-0.07	92.00 [66.00, 125.75]	104.00 [61.75, 130.38]	-0.25	94.56 (46.84)	102.15 (45.65)	-0.16
...Missing; n (%)	27,961 (81.6%)	5,458 (77.1%)	0.11	32,100 (98.6%)	8,150 (98.6%)	0.00	60,061 (89.9%)	13,608 (88.7%)	0.04

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	6,335	1,608		469	122		0	0	
...mean (sd)	183.83 (52.62)	187.10 (48.78)	-0.06	181.89 (60.15)	191.08 (49.85)	-0.17	182.88 (56.42)	189.24 (49.36)	-0.12
...median [IQR]	178.00 [150.00, 211.00]	182.00 [154.00, 216.00]	-0.08	178.00 [145.25, 215.50]	190.00 [158.00, 223.50]	-0.22	178.00 (56.42)	186.31 (49.36)	-0.16
...Missing; n (%)	27,916 (81.5%)	5,470 (77.3%)	0.10	32,096 (98.6%)	8,142 (98.5%)	0.01	60,012 (89.8%)	13,612 (88.7%)	0.04
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	6,217	1,597		470	118		0	0	
...mean (sd)	167.43 (139.68)	173.67 (120.45)	-0.05	192.52 (165.88)	209.43 (138.42)	-0.11	179.66 (153.01)	192.93 (130.44)	-0.09
...median [IQR]	136.00 [97.00, 195.50]	144.50 [105.00, 206.00]	-0.07	157.33 [109.00, 214.50]	167.00 [131.75, 247.75]	-0.06	146.40 (153.01)	156.62 (130.44)	-0.07
...Missing; n (%)	28,034 (81.8%)	5,481 (77.4%)	0.11	32,095 (98.6%)	8,146 (98.6%)	0.00	60,129 (90.0%)	13,627 (88.8%)	0.04
Lab result number- Hemoglobin mean (only >0 included)	6,311	1,527		322	91		0	0	
...mean (sd)	13.63 (1.82)	13.86 (1.78)	-0.13	13.56 (2.07)	111,610.08 (1,048,228.73)	-0.15	13.60 (1.95)	60125.39 (769329.27)	-0.11
...median [IQR]	13.70 [12.40, 14.90]	14.00 [12.67, 15.10]	-0.17	13.70 [12.50, 15.00]	14.30 [13.00, 15.00]	0.00	13.70 (1.95)	14.16 (769329.27)	0.00
...Missing; n (%)	27,940 (81.6%)	5,551 (78.4%)	0.08	32,243 (99.0%)	8,173 (98.9%)	0.01	60,183 (90.1%)	13,724 (89.5%)	0.02
Lab result number- Serum sodium mean (only >90 and <190 included)	8,155	2,011		425	137		0	0	
...mean (sd)	139.83 (2.95)	140.07 (2.79)	-0.08	138.91 (2.74)	139.30 (2.58)	-0.15	139.38 (2.85)	139.66 (2.68)	-0.10
...median [IQR]	140.00 [138.00, 142.00]	140.00 [138.50, 142.00]	0.00	139.00 [137.00, 141.00]	139.50 [137.75, 141.00]	-0.19	139.51 (2.85)	139.73 (2.68)	-0.08
...Missing; n (%)	26,096 (76.2%)	5,067 (71.6%)	0.10	32,140 (98.7%)	8,127 (98.3%)	0.03	58,236 (87.2%)	13,194 (86.0%)	0.04
Lab result number- Albumin mean (only >0 and <=10 included)	7,380	1,825		361	118		0	0	
...mean (sd)	4.16 (0.35)	4.21 (0.34)	-0.14	4.04 (0.65)	4.01 (0.48)	0.05	4.10 (0.52)	4.10 (0.42)	0.00
...median [IQR]	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	0.00	4.10 [4.00, 4.40]	4.00 [4.00, 4.30]	0.18	4.15 (0.52)	4.09 (0.42)	0.13
...Missing; n (%)	26,871 (78.5%)	5,253 (74.2%)	0.10	32,204 (98.9%)	8,146 (98.6%)	0.03	59,075 (88.4%)	13,399 (87.3%)	0.03
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	8,076	2,007		418	139		0	0	
...mean (sd)	131.19 (59.23)	135.47 (61.82)	-0.07	166.36 (68.04)	156.18 (62.58)	0.16	148.33 (63.68)	146.63 (62.23)	0.03
...median [IQR]	110.50 [95.00, 146.38]	114.00 [97.00, 152.50]	-0.06	148.17 [117.50, 193.17]	142.00 [111.00, 188.00]	0.09	128.86 (63.68)	129.08 (62.23)	0.00
...Missing; n (%)	26,175 (76.4%)	5,071 (71.6%)	0.11	32,147 (98.7%)	8,125 (98.3%)	0.03	58,322 (87.3%)	13,196 (86.0%)	0.04
Lab result number- Potassium mean (only 1-7 included)	8,373	2,050		437	133		0	0	
...mean (sd)	4.42 (0.45)	4.46 (0.44)	-0.09	4.32 (0.48)	4.16 (0.44)	0.35	4.37 (0.46)	4.30 (0.44)	0.16
...median [IQR]	4.40 [4.10, 4.70]	4.44 [4.20, 4.70]	-0.09	4.30 [4.00, 4.60]	4.10 [4.00, 4.40]	0.43	4.35 (0.46)	4.26 (0.44)	0.20
...Missing; n (%)	25,878 (75.6%)	5,028 (71.0%)	0.10	32,128 (98.7%)	8,131 (98.4%)	0.03	58,006 (86.8%)	13,159 (85.8%)	0.03
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	4.00 (2.59)	3.69 (2.41)	0.12	2.50 (1.89)	2.21 (1.61)	0.17	3.27 (2.28)	2.89 (2.02)	0.18
...median [IQR]	4.00 [2.00, 6.00]	3.00 [2.00, 5.00]	0.40	2.00 [1.00, 4.00]	2.00 [1.00, 3.00]	0.00	3.03 (2.28)	2.46 (2.02)	0.26
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.20 (0.06)	0.20 (0.05)	0.00	0.18 (0.05)	0.18 (0.04)	0.00	0.19 (0.06)	0.19 (0.04)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...median [IQR]	0.19 [0.17, 0.23]	0.19 [0.16, 0.22]	0.00	0.18 [0.15, 0.20]	0.17 [0.15, 0.19]	0.22	0.19 (0.06)	0.18 (0.04)	0.20
Healthcare Utilization									
Any hospitalization; n (%)	34,191 (99.8%)	7,071 (99.9%)	-0.03	32,565 (100.0%)	8,264 (100.0%)	#DIV/0!	66,756 (99.9%)	15,335 (100.0%)	-0.04
Any hospitalization during prior 31-180 days; n (%)	2,482 (7.2%)	418 (5.9%)	0.05	1,256 (3.9%)	199 (2.4%)	0.09	3,738 (5.6%)	0,617 (4.0%)	0.07
Endocrinologist Visit; n (%)	2,043 (6.0%)	497 (7.0%)	-0.04	1,587 (4.9%)	464 (5.6%)	-0.03	3,630 (5.4%)	0,961 (6.3%)	-0.04
Endocrinologist Visit (30 days prior); n (%)	1,167 (3.4%)	255 (3.6%)	-0.01	910 (2.8%)	244 (3.0%)	-0.01	2,077 (3.1%)	0,499 (3.3%)	-0.01
Endocrinologist Visit (31 to 180 days prior); n (%)	1,161 (3.4%)	321 (4.5%)	-0.06	877 (2.7%)	286 (3.5%)	-0.05	2,038 (3.1%)	0,607 (4.0%)	-0.05
Internal medicine/family medicine visits; n (%)	29,770 (86.9%)	6,033 (85.2%)	0.05	23,203 (71.3%)	5,917 (71.6%)	-0.01	52,973 (79.3%)	11,950 (77.9%)	0.03
Internal medicine/family medicine visits (30 days prior) ; n (%)	25,267 (73.8%)	5,047 (71.3%)	0.06	15,093 (46.3%)	3,669 (44.4%)	0.04	40,360 (60.4%)	8,716 (56.8%)	0.07
Internal medicine/family medicine visits (31 to 180 days prior) ; n (%)	22,710 (66.3%)	4,564 (64.5%)	0.04	18,942 (58.2%)	4,760 (57.6%)	0.01	41,652 (62.3%)	9,324 (60.8%)	0.03
Cardiologist visit; n (%)	31,825 (92.9%)	6,595 (93.2%)	-0.01	12,667 (38.9%)	3,160 (38.2%)	0.01	44,492 (66.6%)	9,755 (63.6%)	0.06
Number of Cardiologist visits (30 days prior); n (%)	31,454 (91.8%)	6,555 (92.6%)	-0.03	10,251 (31.5%)	2,599 (31.4%)	0.00	41,705 (62.4%)	9,154 (59.7%)	0.06
Number of Cardiologist visits (31 to 180 days prior); n (%)	8,575 (25.0%)	1,530 (21.6%)	0.08	4,839 (14.9%)	1,058 (12.8%)	0.06	13,414 (20.1%)	2,588 (16.9%)	0.08
Electrocardiogram ; n (%)	32,129 (93.8%)	6,630 (93.7%)	0.00	19,485 (59.8%)	4,518 (54.7%)	0.10	51,614 (77.2%)	11,148 (72.7%)	0.10
Use of glucose test strips; n (%)	610 (1.8%)	134 (1.9%)	-0.01	427 (1.3%)	124 (1.5%)	-0.02	1,037 (1.6%)	0,258 (1.7%)	-0.01
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
number of different/distinct medication prescriptions									
...mean (sd)	10.48 (5.03)	10.47 (5.09)	0.00	9.73 (4.54)	9.33 (4.39)	0.09	10.11 (4.80)	9.86 (4.73)	0.05
...median [IQR]	10.00 [7.00, 13.00]	10.00 [7.00, 13.00]	0.00	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	0.00	9.51 (4.80)	9.46 (4.73)	0.01
Number of Hospitalizations									
...mean (sd)	1.17 (0.48)	1.13 (0.44)	0.09	1.10 (0.35)	1.06 (0.26)	0.13	1.14 (0.42)	1.09 (0.35)	0.13
...median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 (0.42)	1.00 (0.35)	0.00
Number of hospital days									
...mean (sd)	5.07 (4.30)	4.37 (3.53)	0.18	4.34 (3.10)	3.58 (2.06)	0.29	4.71 (3.76)	3.94 (2.83)	0.23
...median [IQR]	4.00 [3.00, 6.00]	3.00 [3.00, 5.00]	0.25	3.00 [3.00, 5.00]	3.00 [3.00, 4.00]	0.00	3.51 (3.76)	3.00 (2.83)	0.15
Number of Emergency Department (ED) visits									
...mean (sd)	1.26 (1.65)	1.17 (1.73)	0.05	3.03 (5.26)	3.33 (5.85)	-0.05	2.12 (3.86)	2.33 (4.45)	-0.05
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	0.00	2.00 [0.00, 4.00]	2.00 [0.00, 4.00]	0.00	1.49 (3.86)	1.54 (4.45)	-0.01
Number of Office visits									
...mean (sd)	4.08 (3.94)	3.98 (3.73)	0.03	3.39 (3.56)	3.06 (3.22)	0.10	3.74 (3.76)	3.48 (3.46)	0.07
...median [IQR]	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	0.00	2.00 [1.00, 5.00]	2.00 [1.00, 4.00]	0.00	2.51 (3.76)	2.46 (3.46)	0.01
Number of Endocrinologist visits									
...mean (sd)	0.26 (1.62)	0.30 (1.89)	-0.02	0.21 (1.33)	0.24 (1.51)	-0.02	0.75 (1.50)	0.67 (1.62)	0.05
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.51 (1.50)	0.46 (1.62)	0.03
Number of internal medicine/family medicine visits									
...mean (sd)	10.38 (14.10)	9.76 (13.28)	0.05	5.01 (8.06)	4.54 (7.21)	0.06	7.76 (11.56)	6.95 (10.46)	0.07
...median [IQR]	6.00 [2.00, 13.00]	6.00 [2.00, 12.00]	0.00	3.00 [0.00, 6.00]	2.00 [0.00, 6.00]	0.13	4.54 (11.56)	3.85 (10.46)	0.06

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Number of Cardiologist visits									
...mean (sd)	9.25 (6.90)	9.65 (6.77)	-0.06	1.38 (2.87)	1.29 (2.61)	0.03	5.41 (5.33)	5.15 (4.98)	0.05
...median [IQR]	8.00 [5.00, 12.00]	9.00 [6.00, 12.00]	-0.15	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	4.10 (5.33)	4.15 (4.98)	-0.01
Number electrocardiograms received									
...mean (sd)	3.66 (3.02)	3.56 (2.99)	0.03	1.26 (1.60)	1.08 (1.47)	0.12	2.49 (2.43)	2.22 (2.30)	0.11
...median [IQR]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	2.03 (2.43)	1.92 (2.30)	0.05
Number of HbA1c tests ordered									
...mean (sd)	0.47 (0.76)	0.55 (0.79)	-0.10	0.28 (0.60)	0.34 (0.65)	-0.10	0.38 (0.69)	0.44 (0.72)	-0.09
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.00	0.00 (0.69)	0.00 (0.72)	0.00
Number of glucose tests ordered									
...mean (sd)	0.27 (2.79)	0.30 (2.78)	-0.01	0.16 (0.78)	0.16 (0.96)	0.00	0.22 (2.07)	0.22 (2.02)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (2.07)	0.00 (2.02)	0.00
Number of lipid tests ordered									
...mean (sd)	0.58 (0.81)	0.61 (0.80)	-0.04	0.39 (0.83)	0.44 (0.85)	-0.06	0.49 (0.82)	0.52 (0.83)	-0.04
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (0.82)	0.00 (0.83)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.06 (0.33)	0.06 (0.34)	0.00	0.06 (0.33)	0.03 (0.22)	0.11	0.06 (0.33)	0.04 (0.28)	0.07
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.33)	0.00 (0.28)	0.00
Number of BUN tests ordered									
...mean (sd)	0.04 (0.27)	0.04 (0.27)	0.00	0.03 (0.23)	0.02 (0.16)	0.05	0.04 (0.25)	0.03 (0.22)	0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.25)	0.00 (0.22)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.28 (0.78)	0.34 (0.81)	-0.08	0.14 (0.53)	0.16 (0.56)	-0.04	0.21 (0.67)	0.24 (0.69)	-0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.67)	0.00 (0.69)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	11.78 (12.28)	13.43 (11.39)	-0.14	6.46 (8.93)	7.90 (8.45)	-0.17	9.19 (10.78)	10.45 (9.92)	-0.12
...median [IQR]	9.00 [0.00, 18.00]	12.00 [4.00, 19.00]	-0.25	0.00 [0.00, 13.00]	6.00 [0.00, 14.00]	-0.69	4.61 (10.78)	8.77 (9.92)	-0.40
For PS									
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	1,184 (3.5%)	166 (2.3%)	0.07	615 (1.9%)	81 (1.0%)	0.08	1799 (2.7%)	247 (1.6%)	0.08
Occurrence of creatinine tests ordered (for PS); n (%)	1,600 (4.7%)	304 (4.3%)	0.02	1,402 (4.3%)	222 (2.7%)	0.09	3,002 (4.5%)	0,526 (3.4%)	0.06
Occurrence of BUN tests ordered (for PS); n (%)	910 (2.7%)	177 (2.5%)	0.01	786 (2.4%)	120 (1.5%)	0.07	1,696 (2.5%)	0,297 (1.9%)	0.04
Occurrence of chronic renal insufficiency w/o CKD (for PS) ; n (%)	4,154 (12.1%)	710 (10.0%)	0.07	1,526 (4.7%)	247 (3.0%)	0.09	5,680 (8.5%)	0,957 (6.2%)	0.09
Chronic kidney disease Stage 1-2 (for PS); n (%)	1,225 (3.6%)	289 (4.1%)	-0.03	380 (1.2%)	84 (1.0%)	0.02	1605 (2.4%)	373 (2.4%)	0.00
Chronic kidney disease Stage 3-6 (for PS); n (%)	5,711 (16.7%)	1,118 (15.8%)	0.02	2,015 (6.2%)	365 (4.4%)	0.08	7,726 (11.6%)	1,483 (9.7%)	0.06
Bladder stones+Kidney stones (for PS); n (%)	990 (2.9%)	223 (3.2%)	-0.02	535 (1.6%)	151 (1.8%)	-0.02	1,525 (2.3%)	0,374 (2.4%)	-0.01
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) with ICD10 ; n (%)	2,069 (6.0%)	493 (7.0%)	-0.04	735 (2.3%)	166 (2.0%)	0.02	2,804 (4.2%)	0,659 (4.3%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...mean (sd)	1,835.09 (1,422.04)	1,784.22 (1,449.19)	0.04	2,135.45 (1,386.94)	2,271.61 (1,503.12)	-0.09	1981.48 (1405.04)	2046.75 (1478.48)	-0.05
...median [IQR]	1,433.00 [681.00, 2,665.00]	1,315.00 [637.75, 2,606.25]	0.08	1,880.00 [915.00, 3,295.00]	1,999.00 [950.00, 3,558.00]	-0.08	1650.86 (1405.04)	1683.44 (1478.48)	-0.02
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)									
...mean (sd)	23.29 (34.93)	22.94 (32.38)	0.01	18.45 (26.28)	16.63 (21.49)	0.08	20.93 (31.02)	19.54 (27.06)	0.05
...median [IQR]	14.29 [5.85, 29.58]	13.92 [5.00, 29.49]	0.01	12.82 [5.08, 24.33]	10.80 [3.33, 22.51]	0.08	13.57 (31.02)	12.24 (27.06)	0.05
...Missing; n (%)	3,156 (9.2%)	609 (8.6%)	0.02	3,809 (11.7%)	993 (12.0%)	-0.01	6,965 (10.4%)	1602 (10.4%)	0.00
Colonos; n (%)	1,177 (3.4%)	279 (3.9%)	-0.03	991 (3.0%)	292 (3.5%)	-0.03	2,168 (3.2%)	571 (3.7%)	-0.03
Fecal occult blood (FOB) test; n (%)	1,073 (3.1%)	200 (2.8%)	0.02	886 (2.7%)	180 (2.2%)	0.03	1,959 (2.9%)	380 (2.5%)	0.02
Flu vaccine; n (%)	5,381 (15.7%)	1,085 (15.3%)	0.01	3,101 (9.5%)	723 (8.7%)	0.03	8,482 (12.7%)	1808 (11.8%)	0.03
Mammogram; n (%)	2,131 (6.2%)	468 (6.6%)	-0.02	1,397 (4.3%)	322 (3.9%)	0.02	3,528 (5.3%)	790 (5.1%)	0.01
Pap smear; n (%)	485 (1.4%)	114 (1.6%)	-0.02	654 (2.0%)	136 (1.6%)	0.03	1,139 (1.7%)	250 (1.6%)	0.01
Pneumonia vaccine; n (%)	5,203 (15.2%)	1,341 (18.9%)	-0.10	2,015 (6.2%)	721 (8.7%)	-0.10	7,218 (10.8%)	2062 (13.4%)	-0.08
PSA test or Prostate exam for DRE; n (%)	4,519 (13.2%)	1,008 (14.2%)	-0.03	3,148 (9.7%)	932 (11.3%)	-0.05	7,667 (11.5%)	1940 (12.6%)	-0.03
Bone mineral density; n (%)	847 (2.5%)	171 (2.4%)	0.01	371 (1.1%)	87 (1.1%)	0.00	1,218 (1.8%)	258 (1.7%)	0.01
Use of Sympathomimetic agents; n (%)	190 (0.6%)	47 (0.7%)	-0.01	249 (0.8%)	94 (1.1%)	-0.03	0,439 (0.7%)	141 (0.9%)	-0.02
Use of CNS stimulants; n (%)	102 (0.3%)	24 (0.3%)	0.00	162 (0.5%)	48 (0.6%)	-0.01	0,264 (0.4%)	72 (0.5%)	-0.01
Use of estrogens, progestins, androgens; n (%)	845 (2.5%)	197 (2.8%)	-0.02	1,332 (4.1%)	328 (4.0%)	0.01	2,177 (3.3%)	525 (3.4%)	-0.01
Use of Angiogenesis inhibitors; n (%)	17 (0.0%)	5 (0.1%)	-0.04	0 (0.0%)	1 (0.0%)	#DIV/0!	0,017 (0.0%)	6 (0.0%)	#DIV/0!
Use of Oral Immunosuppressants; n (%)	52 (0.2%)	15 (0.2%)	0.00	75 (0.2%)	22 (0.3%)	-0.02	0,127 (0.2%)	37 (0.2%)	0.00
Use of fondaparinux or Bivalirudin; n (%)	3 (0.0%)	0 (0.0%)	#DIV/0!	9 (0.0%)	0 (0.0%)	#DIV/0!	0,012 (0.0%)	0 (0.0%)	#DIV/0!
Use of other direct thrombin inhibitors (lepirudin, desirudin, argatroban); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0 (0.0%)	#DIV/0!
Use of Prasugrel ON CED; n (%)	148 (0.4%)	29 (0.4%)	0.00	155 (0.5%)	34 (0.4%)	0.01	0,303 (0.5%)	63 (0.4%)	0.01
Use of Prasugrel 180 to 1 day prior; n (%)	213 (0.6%)	65 (0.9%)	-0.03	205 (0.6%)	59 (0.7%)	-0.01	0,418 (0.6%)	124 (0.8%)	-0.02
Duration of index hospitalization (i.e. anchor hospitalization LOS)									
...mean (sd)	4.54 (3.88)	3.98 (3.03)	0.16	3.97 (2.44)	3.38 (1.57)	0.29	4.26 (3.26)	3.66 (2.36)	0.21
...median [IQR]	4.00 [3.00, 5.00]	3.00 [3.00, 4.00]	0.29	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.51 (3.26)	3.00 (2.36)	0.18
Number of D-dimer tests									
...mean (sd)	0.04 (0.23)	0.04 (0.23)	0.00	0.05 (0.23)	0.06 (0.26)	-0.04	0.04 (0.23)	0.05 (0.25)	-0.04
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.23)	0.00 (0.25)	0.00
Number of CRP, high-sensitivity CRP tests									
...mean (sd)	0.06 (0.33)	0.06 (0.30)	0.00	0.04 (0.27)	0.04 (0.27)	0.00	0.05 (0.30)	0.05 (0.28)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.30)	0.00 (0.28)	0.00
Number of PT or aPTT tests									
...mean (sd)	0.59 (1.97)	0.40 (1.37)	0.11	0.48 (1.37)	0.37 (0.98)	0.09	0.54 (1.70)	0.38 (1.18)	0.11
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.70)	0.00 (1.18)	0.00
Number of Bleeding time tests									
...mean (sd)	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.02)	0.00 (0.02)	0.00	0.00 (0.02)	0.00 (0.02)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.02)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days									
...mean (sd)	4.05 (0.76)	3.90 (0.75)	0.20	3.57 (0.66)	3.36 (0.59)	0.34	3.82 (0.71)	3.61 (0.67)	0.30

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...median [IQR]	4.00 [4.00, 4.00]	4.00 [3.00, 4.00]	0.00	4.00 [3.00, 4.00]	3.00 [3.00, 4.00]	1.60	4.00 (0.71)	3.46 (0.67)	0.78
Drug eluting stent; n (%)	8,430 (24.6%)	1,218 (17.2%)	0.18	10,014 (30.8%)	2,371 (28.7%)	0.05	18,444 (27.6%)	3589 (23.4%)	0.10
Bare metal stent; n (%)	18,447 (53.9%)	5,947 (84.0%)	-0.69	15,203 (46.7%)	7,011 (84.8%)	-0.88	33,650 (50.4%)	12958 (84.5%)	-0.78
Use of CYP inhibitors; n (%)	7,802 (22.8%)	1,443 (20.4%)	0.06	6,227 (19.1%)	1,374 (16.6%)	0.07	14,029 (21.0%)	2817 (18.4%)	0.07
Use of CYP inducers; n (%)	41 (0.1%)	7 (0.1%)	0.00	64 (0.2%)	9 (0.1%)	0.03	0,105 (0.2%)	16 (0.1%)	0.03
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - TRUVEN									
...Commercial; n (%)	9,219 (26.9%)	2,194 (31.0%)	-0.09	15,361 (47.2%)	2,555 (30.9%)	0.34	24,580 (36.8%)	4749 (31.0%)	0.12
...Medicare Advantage; n (%)	25,032 (73.1%)	4,884 (69.0%)	0.09	17,204 (52.8%)	5,709 (69.1%)	-0.34	42,236 (63.2%)	10593 (69.0%)	-0.12
Commercial vs Medicare Advantage- Business Type Code									
...COM = COMMERCIAL; n (%)	9,219 (26.9%)	2,194 (31.0%)	-0.09	-	-	#VALUE!	9,219 (26.9%)	2,194 (31.0%)	-0.09
...MCR = MEDICARE; n (%)	25,032 (73.1%)	4,884 (69.0%)	0.09	-	-	#VALUE!	25,032 (73.1%)	4,884 (69.0%)	0.09
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type									
...1 - Fee For Service; n (%)	-	-	#VALUE!	15,223 (46.7%)	5,158 (62.4%)	-0.32	15,223 (46.7%)	5,158 (62.4%)	-0.32
...2 - Encounter; n (%)	-	-	#VALUE!	1,981 (6.1%)	551 (6.7%)	-0.02	1,981 (6.1%)	551 (6.7%)	-0.02
...3 - Medicare; n (%)	-	-	#VALUE!	13,443 (41.3%)	2,290 (27.7%)	0.29	13,443 (41.3%)	2,290 (27.7%)	0.29
...4 - Medicare Encounter; n (%)	-	-	#VALUE!	1,918 (5.9%)	265 (3.2%)	0.13	1,918 (5.9%)	265 (3.2%)	0.13
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)									
...Urban; n (%)	-	-	#VALUE!	23,495 (72.1%)	5,859 (70.9%)	0.03	23,495 (72.1%)	5,859 (70.9%)	0.03
...Rural; n (%)	-	-	#VALUE!	1,316 (4.0%)	628 (7.6%)	-0.15	1,316 (4.0%)	628 (7.6%)	-0.15
...Unknown/Missing; n (%)	-	-	#VALUE!	7,754 (23.8%)	1,777 (21.5%)	0.05497	7,754 (23.8%)	1,777 (21.5%)	0.05
N of Generic name drugs									
...mean (sd)	17.06 (13.53)	15.92 (13.38)	0.08	13.50 (10.40)	12.08 (9.64)	0.14	15.32 (12.11)	13.85 (11.52)	0.12
...median [IQR]	14.00 [8.00, 22.00]	12.00 [7.00, 21.00]	0.15	11.00 [6.00, 18.00]	10.00 [5.00, 16.00]	0.10	12.54 (12.11)	10.92 (11.52)	0.14
N of Brand name drugs									
...mean (sd)	3.13 (4.46)	3.86 (4.39)	-0.16	3.48 (4.24)	3.82 (3.89)	-0.08	3.30 (4.35)	3.84 (4.13)	-0.13
...median [IQR]	1.00 [0.00, 4.00]	2.00 [1.00, 5.00]	-0.226	2.00 [1.00, 5.00]	2.00 [1.00, 5.00]	0	1.49 (4.35)	2.00 (4.13)	-0.12

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

PS-matched									
Variable	Optum			Truven			POOLED		
	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.	Clopidogrel 75mg	Ticagrelor 90mg	St. Diff.
Number of patients	6,697	6,697		7,283	7,283		13,980	13,980	
Age									
...mean (sd)	68.19 (10.96)	68.38 (10.66)	-0.02	62.57 (11.12)	62.72 (10.33)	-0.01	65.26 (11.04)	65.43 (10.49)	-0.02
...median [IQR]	69.00 [61.00, 76.00]	69.00 [62.00, 76.00]	0.00	62.00 [56.00, 62.00]	62.00 [57.00, 62.00]	0.00	65.35 (11.04)	65.35 (10.49)	0.00
Age categories									
...18 - 54; n (%)	761 (11.4%)	716 (10.7%)	0.02	1,548 (21.3%)	1,372 (18.8%)	0.06	2,309 (16.5%)	2,088 (14.9%)	0.04
...55 - 64; n (%)	1,531 (22.9%)	1,473 (22.0%)	0.02	3,310 (45.4%)	3,451 (47.4%)	-0.04	4,841 (34.6%)	4,924 (35.2%)	-0.01
...65 - 74; n (%)	2,461 (36.7%)	2,515 (37.6%)	-0.02	1,339 (18.4%)	1,446 (19.9%)	-0.04	3,800 (27.2%)	3,961 (28.3%)	-0.02
...≥ 75; n (%)	1,944 (29.0%)	1,993 (29.8%)	-0.02	1,086 (14.9%)	1,014 (13.9%)	0.03	3,030 (21.7%)	3,007 (21.5%)	0.00
Gender									
...Males; n (%)	4,290 (64.1%)	4,277 (63.9%)	0.00	5,161 (70.9%)	5,145 (70.6%)	0.01	9,451 (67.6%)	9,422 (67.4%)	0.00
...Females; n (%)	2,407 (35.9%)	2,420 (36.1%)	0.00	2,122 (29.1%)	2,138 (29.4%)	-0.01	4,529 (32.4%)	4,558 (32.6%)	0.00
Region									
...Northeast; n (%)	777 (11.6%)	772 (11.5%)	0.00	1,356 (18.6%)	1,386 (19.0%)	-0.01	2,133 (15.3%)	2,158 (15.4%)	0.00
...South; n (%)	3,136 (46.8%)	3,102 (46.3%)	0.01	2,027 (27.8%)	2,009 (27.6%)	0.00	5,163 (36.9%)	5,111 (36.6%)	0.01
...Midwest; n (%)	1,524 (22.8%)	1,566 (23.4%)	-0.01	3,064 (42.1%)	3,047 (41.8%)	0.01	4,588 (32.8%)	4,613 (33.0%)	0.00
...West; n (%)	1,260 (18.8%)	1,257 (18.8%)	0.00	796 (10.9%)	803 (11.0%)	0.00	2,056 (14.7%)	2,060 (14.7%)	0.00
...Unknown+missing; n (%)	N/A	N/A	#VALUE!	40 (0.5%)	38 (0.5%)	0.00	40 (0.3%)	38 (0.3%)	0.00
CV Covariates									
Ischemic heart disease; n (%)	6,697 (100.0%)	6,697 (100.0%)	#DIV/0!	7,283 (100.0%)	7,283 (100.0%)	#DIV/0!	13,980 (100.0%)	13,980 (100.0%)	#DIV/0!
Acute MI; n (%)	6,135 (91.6%)	6,128 (91.5%)	0.00	6,879 (94.5%)	6,876 (94.4%)	0.00	13014 (93.1%)	13004 (93.0%)	0.00
ACS/unstable angina; n (%)	2,839 (42.4%)	2,840 (42.4%)	0.00	2,601 (35.7%)	2,637 (36.2%)	-0.01	5440 (38.9%)	5477 (39.2%)	-0.01
Old MI; n (%)	1,126 (16.8%)	1,128 (16.8%)	0.00	684 (9.4%)	652 (9.0%)	0.01	1810 (12.9%)	1780 (12.7%)	0.01
Stable angina; n (%)	1,622 (24.2%)	1,691 (25.3%)	-0.03	1,196 (16.4%)	1,199 (16.5%)	0.00	2,818 (20.2%)	2,890 (20.7%)	-0.01
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	6,437 (96.1%)	6,433 (96.1%)	0.00	6,745 (92.6%)	6,733 (92.4%)	0.01	13,182 (94.3%)	13,166 (94.2%)	0.00
Other atherosclerosis with ICD10 ; n (%)	86 (1.3%)	81 (1.2%)	0.01	98 (1.3%)	85 (1.2%)	0.01	184 (1.3%)	166 (1.2%)	0.01
Previous cardiac procedure (CABG or PTCA or Stent); n (%)	6,024 (90.0%)	6,183 (92.3%)	-0.08	6,519 (89.5%)	6,549 (89.9%)	-0.01	12543 (89.7%)	12732 (91.1%)	-0.05
History of CABG or PTCA; n (%)	2,490 (37.2%)	2,351 (35.1%)	0.04	1,494 (20.5%)	1,309 (18.0%)	0.06	3,984 (28.5%)	3,660 (26.2%)	0.05
Any stroke; n (%)	622 (9.3%)	601 (9.0%)	0.01	406 (5.6%)	416 (5.7%)	0.00	1,028 (7.4%)	1,017 (7.3%)	0.00
Ischemic stroke (w and w/o mention of cerebral infarction); n (%)	616 (9.2%)	598 (8.9%)	0.01	406 (5.6%)	416 (5.7%)	0.00	1,022 (7.3%)	1,014 (7.3%)	0.00
Hemorrhagic stroke; n (%)	13 (0.2%)	7 (0.1%)	0.03	0 (0.0%)	0 (0.0%)	#DIV/0!	13 (0.1%)	7 (0.1%)	0.00
TIA; n (%)	120 (1.8%)	125 (1.9%)	-0.01	83 (1.1%)	77 (1.1%)	0.00	203 (1.5%)	202 (1.4%)	0.01
Other cerebrovascular disease; n (%)	143 (2.1%)	151 (2.3%)	-0.01	72 (1.0%)	73 (1.0%)	0.00	215 (1.5%)	224 (1.6%)	-0.01
Late effects of cerebrovascular disease; n (%)	134 (2.0%)	135 (2.0%)	0.00	51 (0.7%)	50 (0.7%)	0.00	185 (1.3%)	185 (1.3%)	0.00
Cerebrovascular procedure; n (%)	8 (0.1%)	8 (0.1%)	0.00	7 (0.1%)	4 (0.1%)	0.00	15 (0.1%)	12 (0.1%)	0.00
Heart failure (CHF); n (%)	1,722 (25.7%)	1,720 (25.7%)	0.00	1,134 (15.6%)	1,134 (15.6%)	0.00	2,856 (20.4%)	2,854 (20.4%)	0.00
Peripheral Vascular Disease (PVD) or PVD Surgery ; n (%)	874 (13.1%)	843 (12.6%)	0.01	397 (5.5%)	394 (5.4%)	0.00	1,271 (9.1%)	1,237 (8.8%)	0.01
Atrial fibrillation; n (%)	815 (12.2%)	823 (12.3%)	0.00	598 (8.2%)	561 (7.7%)	0.02	1,413 (10.1%)	1,384 (9.9%)	0.01
Other cardiac dysrhythmia; n (%)	2,463 (36.8%)	2,524 (37.7%)	-0.02	2,216 (30.4%)	2,204 (30.3%)	0.00	4,679 (33.5%)	4,728 (33.8%)	-0.01

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Cardiac conduction disorders; n (%)	1,075 (16.1%)	1,041 (15.5%)	0.02	749 (10.3%)	748 (10.3%)	0.00	1824 (13.0%)	1789 (12.8%)	0.01
Other CVD; n (%)	2,475 (37.0%)	2,563 (38.3%)	-0.03	1,945 (26.7%)	1,998 (27.4%)	-0.02	4,420 (31.6%)	4,561 (32.6%)	-0.02
Diabetes-related complications									
Diabetic retinopathy; n (%)	267 (4.0%)	253 (3.8%)	0.01	144 (2.0%)	132 (1.8%)	0.01	0,411 (2.9%)	0,385 (2.8%)	0.01
Diabetes with other ophthalmic manifestations; n (%)	25 (0.4%)	36 (0.5%)	-0.01	67 (0.9%)	63 (0.9%)	0.00	0,092 (0.7%)	0,099 (0.7%)	0.00
Retinal detachment, vitreous hemorrhage, vitrectomy; n (%)	28 (0.4%)	15 (0.2%)	0.04	21 (0.3%)	21 (0.3%)	0.00	49 (0.4%)	36 (0.3%)	0.02
Retinal laser coagulation therapy; n (%)	27 (0.4%)	28 (0.4%)	0.00	34 (0.5%)	30 (0.4%)	0.01	61 (0.4%)	58 (0.4%)	0.00
Occurrence of Diabetic Neuropathy ; n (%)	871 (13.0%)	833 (12.4%)	0.02	389 (5.3%)	371 (5.1%)	0.01	1,260 (9.0%)	1,204 (8.6%)	0.01
Occurrence of diabetic nephropathy with ICD10 ; n (%)	814 (12.2%)	805 (12.0%)	0.01	220 (3.0%)	224 (3.1%)	-0.01	1,034 (7.4%)	1,029 (7.4%)	0.00
Hypoglycemia ; n (%)	56 (0.8%)	40 (0.6%)	0.02	97 (1.3%)	91 (1.2%)	0.01	0,153 (1.1%)	0,131 (0.9%)	0.02
Hyperglycemia; n (%)	600 (9.0%)	604 (9.0%)	0.00	444 (6.1%)	442 (6.1%)	0.00	1,044 (7.5%)	1,046 (7.5%)	0.00
Disorders of fluid electrolyte and acid-base balance; n (%)	1,318 (19.7%)	1,332 (19.9%)	-0.01	681 (9.4%)	709 (9.7%)	-0.01	1,999 (14.3%)	2,041 (14.6%)	-0.01
Diabetic ketoacidosis; n (%)	43 (0.6%)	35 (0.5%)	0.01	45 (0.6%)	43 (0.6%)	0.00	88 (0.6%)	78 (0.6%)	0.00
Hyperosmolar hyperglycemic nonketotic syndrome (HONK); n (%)	31 (0.5%)	32 (0.5%)	0.00	12 (0.2%)	12 (0.2%)	0.00	43 (0.3%)	44 (0.3%)	0.00
Diabetes with peripheral circulatory disorders with ICD-10 ; n (%)	444 (6.6%)	441 (6.6%)	0.00	132 (1.8%)	127 (1.7%)	0.01	0,576 (4.1%)	0,568 (4.1%)	0.00
Diabetic Foot; n (%)	105 (1.6%)	101 (1.5%)	0.01	67 (0.9%)	67 (0.9%)	0.00	172 (1.2%)	168 (1.2%)	0.00
Gangrene ; n (%)	10 (0.1%)	9 (0.1%)	0.00	8 (0.1%)	3 (0.0%)	0.04	18 (0.1%)	12 (0.1%)	0.00
Lower extremity amputation; n (%)	50 (0.7%)	45 (0.7%)	0.00	12 (0.2%)	14 (0.2%)	0.00	62 (0.4%)	59 (0.4%)	0.00
Osteomyelitis; n (%)	23 (0.3%)	29 (0.4%)	-0.02	13 (0.2%)	19 (0.3%)	-0.02	36 (0.3%)	48 (0.3%)	0.00
Skin infections ; n (%)	309 (4.6%)	313 (4.7%)	0.00	252 (3.5%)	253 (3.5%)	0.00	0,561 (4.0%)	0,566 (4.0%)	0.00
Erectile dysfunction; n (%)	208 (3.1%)	216 (3.2%)	-0.01	182 (2.5%)	179 (2.5%)	0.00	0,390 (2.8%)	0,395 (2.8%)	0.00
Diabetes with unspecified complication; n (%)	373 (5.6%)	364 (5.4%)	0.01	225 (3.1%)	216 (3.0%)	0.01	0,598 (4.3%)	0,580 (4.1%)	0.01
Diabetes mellitus without mention of complications; n (%)	3,495 (52.2%)	3,487 (52.1%)	0.00	2,994 (41.1%)	2,965 (40.7%)	0.01	6,489 (46.4%)	6,452 (46.2%)	0.00
Hypertension: 1 inpatient or 2 outpatient claims within 365 days; n (%)	5,783 (86.4%)	5,821 (86.9%)	-0.01	5,612 (77.1%)	5,617 (77.1%)	0.00	11,395 (81.5%)	11,438 (81.8%)	-0.01
Hyperlipidemia ; n (%)	5,592 (83.5%)	5,633 (84.1%)	-0.02	5,162 (70.9%)	5,159 (70.8%)	0.00	10,754 (76.9%)	10,792 (77.2%)	-0.01
Edema; n (%)	447 (6.7%)	442 (6.6%)	0.00	214 (2.9%)	220 (3.0%)	-0.01	0,661 (4.7%)	0,662 (4.7%)	0.00
Renal Dysfunction (non-diabetic) ; n (%)	2,007 (30.0%)	2,049 (30.6%)	-0.01	999 (13.7%)	969 (13.3%)	0.01	3,006 (21.5%)	3,018 (21.6%)	0.00
Occurrence of acute renal disease ; n (%)	928 (13.9%)	919 (13.7%)	0.01	419 (5.8%)	425 (5.8%)	0.00	1347 (9.6%)	1344 (9.6%)	0.00
Occurrence of chronic renal insufficiency; n (%)	1,520 (22.7%)	1,503 (22.4%)	0.01	534 (7.3%)	520 (7.1%)	0.01	2,054 (14.7%)	2,023 (14.5%)	0.01
Chronic kidney disease ; n (%)	1,486 (22.2%)	1,464 (21.9%)	0.01	516 (7.1%)	494 (6.8%)	0.01	2,002 (14.3%)	1,958 (14.0%)	0.01
CKD Stage 3-4; n (%)	1,056 (15.8%)	1,045 (15.6%)	0.01	336 (4.6%)	330 (4.5%)	0.00	1,392 (10.0%)	1,375 (9.8%)	0.01
Occurrence of hypertensive nephropathy; n (%)	1,199 (17.9%)	1,177 (17.6%)	0.01	362 (5.0%)	363 (5.0%)	0.00	1561 (11.2%)	1540 (11.0%)	0.01
Occurrence of miscellaneous renal insufficiency ; n (%)	580 (8.7%)	598 (8.9%)	-0.01	306 (4.2%)	307 (4.2%)	0.00	0,886 (6.3%)	0,905 (6.5%)	-0.01
Glaucoma or cataracts ; n (%)	1,046 (15.6%)	1,061 (15.8%)	-0.01	817 (11.2%)	798 (11.0%)	0.01	1,863 (13.3%)	1,859 (13.3%)	0.00
Cellulitis or abscess of toe; n (%)	94 (1.4%)	82 (1.2%)	0.02	38 (0.5%)	47 (0.6%)	-0.01	132 (0.9%)	129 (0.9%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Foot ulcer; n (%)	107 (1.6%)	104 (1.6%)	0.00	63 (0.9%)	67 (0.9%)	0.00	170 (1.2%)	171 (1.2%)	0.00
Bladder stones; n (%)	13 (0.2%)	8 (0.1%)	0.03	9 (0.1%)	8 (0.1%)	0.00	22 (0.2%)	16 (0.1%)	0.03
Kidney stones; n (%)	218 (3.3%)	207 (3.1%)	0.01	127 (1.7%)	120 (1.6%)	0.01	0,345 (2.5%)	0,327 (2.3%)	0.01
Urinary tract infections (UTIs); n (%)	588 (8.8%)	597 (8.9%)	0.00	291 (4.0%)	280 (3.8%)	0.01	0,879 (6.3%)	0,877 (6.3%)	0.00
Dipstick urinalysis; n (%)	1,825 (27.3%)	1,872 (28.0%)	-0.02	1,486 (20.4%)	1,441 (19.8%)	0.01	3,311 (23.7%)	3,313 (23.7%)	0.00
Non-dipstick urinalysis; n (%)	1,275 (19.0%)	1,303 (19.5%)	-0.01	748 (10.3%)	734 (10.1%)	0.01	2,023 (14.5%)	2,037 (14.6%)	0.00
Urine function test; n (%)	148 (2.2%)	152 (2.3%)	-0.01	116 (1.6%)	132 (1.8%)	-0.02	0,264 (1.9%)	0,284 (2.0%)	-0.01
Cytology; n (%)	69 (1.0%)	83 (1.2%)	-0.02	25 (0.3%)	32 (0.4%)	-0.02	94 (0.7%)	115 (0.8%)	-0.01
Cystos; n (%)	102 (1.5%)	103 (1.5%)	0.00	57 (0.8%)	36 (0.5%)	0.04	159 (1.1%)	139 (1.0%)	0.01
Other Covariates									
Liver disease; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0,000 (0.0%)	#DIV/0!
Osteoarthritis; n (%)	1,393 (20.8%)	1,383 (20.7%)	0.00	848 (11.6%)	881 (12.1%)	-0.02	2,241 (16.0%)	2,264 (16.2%)	-0.01
Other arthritis, arthropathies and musculoskeletal pain; n (%)	2,587 (38.6%)	2,593 (38.7%)	0.00	2,193 (30.1%)	2,215 (30.4%)	-0.01	4,780 (34.2%)	4,808 (34.4%)	0.00
Dorsopathies; n (%)	1,774 (26.5%)	1,745 (26.1%)	0.01	1,480 (20.3%)	1,469 (20.2%)	0.00	3,254 (23.3%)	3,214 (23.0%)	0.01
Fractures; n (%)	206 (3.1%)	195 (2.9%)	0.01	132 (1.8%)	137 (1.9%)	-0.01	0,338 (2.4%)	0,332 (2.4%)	0.00
Falls; n (%)	255 (3.8%)	255 (3.8%)	0.00	73 (1.0%)	66 (0.9%)	0.01	328 (2.3%)	321 (2.3%)	0.00
Osteoporosis; n (%)	310 (4.6%)	314 (4.7%)	0.00	155 (2.1%)	156 (2.1%)	0.00	0,465 (3.3%)	0,470 (3.4%)	-0.01
Hyperthyroidism; n (%)	33 (0.5%)	45 (0.7%)	-0.03	22 (0.3%)	22 (0.3%)	0.00	55 (0.4%)	67 (0.5%)	-0.01
Hypothyroidism ; n (%)	1,142 (17.1%)	1,098 (16.4%)	0.02	706 (9.7%)	734 (10.1%)	-0.01	1,848 (13.2%)	1,832 (13.1%)	0.00
Other disorders of thyroid gland ; n (%)	203 (3.0%)	236 (3.5%)	-0.03	174 (2.4%)	164 (2.3%)	0.01	0,377 (2.7%)	0,400 (2.9%)	-0.01
Depression; n (%)	779 (11.6%)	782 (11.7%)	0.00	449 (6.2%)	458 (6.3%)	0.00	1,228 (8.8%)	1,240 (8.9%)	0.00
Anxiety; n (%)	947 (14.1%)	939 (14.0%)	0.00	586 (8.0%)	601 (8.3%)	-0.01	1,533 (11.0%)	1,540 (11.0%)	0.00
SleepDisorder; n (%)	301 (4.5%)	316 (4.7%)	-0.01	466 (6.4%)	439 (6.0%)	0.02	0,767 (5.5%)	0,755 (5.4%)	0.00
Dementia; n (%)	292 (4.4%)	303 (4.5%)	0.00	112 (1.5%)	119 (1.6%)	-0.01	404 (2.9%)	422 (3.0%)	-0.01
Delirium; n (%)	162 (2.4%)	155 (2.3%)	0.01	65 (0.9%)	67 (0.9%)	0.00	227 (1.6%)	222 (1.6%)	0.00
Psychosis; n (%)	67 (1.0%)	61 (0.9%)	0.01	32 (0.4%)	34 (0.5%)	-0.01	99 (0.7%)	95 (0.7%)	0.00
Obesity; n (%)	1,796 (26.8%)	1,832 (27.4%)	-0.01	1,445 (19.8%)	1,357 (18.6%)	0.03	3,241 (23.2%)	3,189 (22.8%)	0.01
Overweight; n (%)	484 (7.2%)	489 (7.3%)	0.00	218 (3.0%)	217 (3.0%)	0.00	0,702 (5.0%)	0,706 (5.1%)	0.00
Smoking; n (%)	3,128 (46.7%)	3,124 (46.6%)	0.00	2,083 (28.6%)	2,118 (29.1%)	-0.01	5,211 (37.3%)	5,242 (37.5%)	0.00
Alcohol abuse or dependence; n (%)	152 (2.3%)	159 (2.4%)	-0.01	108 (1.5%)	114 (1.6%)	-0.01	260 (1.9%)	273 (2.0%)	-0.01
Drug abuse or dependence; n (%)	195 (2.9%)	188 (2.8%)	0.01	91 (1.2%)	94 (1.3%)	-0.01	286 (2.0%)	282 (2.0%)	0.00
COPD; n (%)	1,228 (18.3%)	1,230 (18.4%)	0.00	671 (9.2%)	640 (8.8%)	0.01	1,899 (13.6%)	1,870 (13.4%)	0.01
Asthma; n (%)	484 (7.2%)	494 (7.4%)	-0.01	363 (5.0%)	369 (5.1%)	0.00	0,847 (6.1%)	0,863 (6.2%)	0.00
Obstructive sleep apnea; n (%)	770 (11.5%)	783 (11.7%)	-0.01	630 (8.7%)	612 (8.4%)	0.01	1,400 (10.0%)	1,395 (10.0%)	0.00
Pneumonia; n (%)	425 (6.3%)	456 (6.8%)	-0.02	198 (2.7%)	219 (3.0%)	-0.02	0,623 (4.5%)	0,675 (4.8%)	-0.01
Imaging; n (%)	211 (3.2%)	203 (3.0%)	0.01	80 (1.1%)	101 (1.4%)	-0.03	291 (2.1%)	304 (2.2%)	-0.01
Other Medications									
Use of ACE inhibitors; n (%)	3,488 (52.1%)	3,508 (52.4%)	-0.01	4,129 (56.7%)	4,130 (56.7%)	0.00	7,617 (54.5%)	7,638 (54.6%)	0.00
Use of ARBs; n (%)	1,623 (24.2%)	1,647 (24.6%)	-0.01	1,544 (21.2%)	1,551 (21.3%)	0.00	3,167 (22.7%)	3,198 (22.9%)	0.00
Use of Loop Diuretics- ; n (%)	1,034 (15.4%)	1,025 (15.3%)	0.00	580 (8.0%)	588 (8.1%)	0.00	1,614 (11.5%)	1,613 (11.5%)	0.00
Use of other diuretics- ; n (%)	318 (4.7%)	327 (4.9%)	-0.01	322 (4.4%)	302 (4.1%)	0.01	0,640 (4.6%)	0,629 (4.5%)	0.00
Use of nitrates- ; n (%)	2,918 (43.6%)	2,928 (43.7%)	0.00	3,267 (44.9%)	3,251 (44.6%)	0.01	6,185 (44.2%)	6,179 (44.2%)	0.00
Use of other hypertension drugs; n (%)	518 (7.7%)	509 (7.6%)	0.00	352 (4.8%)	353 (4.8%)	0.00	0,870 (6.2%)	0,862 (6.2%)	0.00
Use of digoxin- ; n (%)	72 (1.1%)	71 (1.1%)	0.00	70 (1.0%)	62 (0.9%)	0.01	142 (1.0%)	133 (1.0%)	0.00
Use of Anti-arrhythmics; n (%)	178 (2.7%)	204 (3.0%)	-0.02	159 (2.2%)	154 (2.1%)	0.01	337 (2.4%)	358 (2.6%)	-0.01
Use of COPD/asthma meds- ; n (%)	1,024 (15.3%)	1,023 (15.3%)	0.00	885 (12.2%)	894 (12.3%)	0.00	1,909 (13.7%)	1,917 (13.7%)	0.00
Use of statins; n (%)	6,026 (90.0%)	6,037 (90.1%)	0.00	6,668 (91.6%)	6,661 (91.5%)	0.00	12,694 (90.8%)	12,698 (90.8%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Use of other lipid-lowering drugs; n (%)	504 (7.5%)	511 (7.6%)	0.00	660 (9.1%)	658 (9.0%)	0.00	1,164 (8.3%)	1,169 (8.4%)	0.00
Use of oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Warfarin); n (%)	367 (5.5%)	349 (5.2%)	0.01	346 (4.8%)	312 (4.3%)	0.02	0,713 (5.1%)	0,661 (4.7%)	0.02
Use of heparin and other low-molecular weight heparins; n (%)	37 (0.6%)	41 (0.6%)	0.00	0 (0.0%)	0 (0.0%)	#DIV/0!	37 (0.3%)	41 (0.3%)	0.00
Use of NSAIDs; n (%)	997 (14.9%)	1,014 (15.1%)	-0.01	1,127 (15.5%)	1,115 (15.3%)	0.01	2,124 (15.2%)	2,129 (15.2%)	0.00
Use of oral corticosteroids; n (%)	1,231 (18.4%)	1,215 (18.1%)	0.01	1,145 (15.7%)	1,119 (15.4%)	0.01	2,376 (17.0%)	2,334 (16.7%)	0.01
Use of bisphosphonate (); n (%)	113 (1.7%)	108 (1.6%)	0.01	69 (0.9%)	64 (0.9%)	0.00	182 (1.3%)	172 (1.2%)	0.01
Use of opioids-; n (%)	1,663 (24.8%)	1,668 (24.9%)	0.00	1,603 (22.0%)	1,582 (21.7%)	0.01	3,266 (23.4%)	3,250 (23.2%)	0.00
Use of antidepressants; n (%)	1,356 (20.2%)	1,338 (20.0%)	0.00	1,158 (15.9%)	1,165 (16.0%)	0.00	2,514 (18.0%)	2,503 (17.9%)	0.00
Use of antipsychotics; n (%)	128 (1.9%)	139 (2.1%)	-0.01	63 (0.9%)	68 (0.9%)	0.00	0,191 (1.4%)	0,207 (1.5%)	-0.01
Use of anticonvulsants; n (%)	975 (14.6%)	907 (13.5%)	0.03	612 (8.4%)	577 (7.9%)	0.02	1,587 (11.4%)	1,484 (10.6%)	0.03
Use of lithium-; n (%)	10 (0.1%)	11 (0.2%)	-0.03	6 (0.1%)	6 (0.1%)	0.00	16 (0.1%)	17 (0.1%)	0.00
Use of Benzos-; n (%)	792 (11.8%)	764 (11.4%)	0.01	761 (10.4%)	742 (10.2%)	0.01	1,553 (11.1%)	1,506 (10.8%)	0.01
Use of anxiolytics/hypnotics-; n (%)	310 (4.6%)	306 (4.6%)	0.00	399 (5.5%)	381 (5.2%)	0.01	0,709 (5.1%)	0,687 (4.9%)	0.01
Use of dementia meds-; n (%)	118 (1.8%)	121 (1.8%)	0.00	60 (0.8%)	59 (0.8%)	0.00	178 (1.3%)	180 (1.3%)	0.00
Use of antiparkinsonian meds-; n (%)	154 (2.3%)	147 (2.2%)	0.01	100 (1.4%)	103 (1.4%)	0.00	0,254 (1.8%)	0,250 (1.8%)	0.00
Entresto (sacubitril/valsartan); n (%)	15 (0.2%)	16 (0.2%)	0.00	6 (0.1%)	3 (0.0%)	0.04	21 (0.2%)	19 (0.1%)	0.03
Labs									
Lab values- HbA1c (%) ; n (%)	1,404 (21.0%)	1,381 (20.6%)	0.01	128 (1.8%)	103 (1.4%)	0.03	1,532 (11.0%)	1,484 (10.6%)	0.01
Lab values- HbA1c (%) (within 3 months); n (%)	920 (13.7%)	888 (13.3%)	0.01	75 (1.0%)	74 (1.0%)	0.00	0,995 (7.1%)	0,962 (6.9%)	0.01
Lab values- HbA1c (%) (within 6 months); n (%)	1,404 (21.0%)	1,381 (20.6%)	0.01	128 (1.8%)	103 (1.4%)	0.03	1,532 (11.0%)	1,484 (10.6%)	0.01
Lab values- BNP; n (%)	87 (1.3%)	74 (1.1%)	0.02	10 (0.1%)	2 (0.0%)	0.04	97 (0.7%)	76 (0.5%)	0.03
Lab values- BNP (within 3 months); n (%)	72 (1.1%)	53 (0.8%)	0.03	7 (0.1%)	1 (0.0%)	0.04	79 (0.6%)	54 (0.4%)	0.03
Lab values- BNP (within 6 months); n (%)	87 (1.3%)	74 (1.1%)	0.02	10 (0.1%)	2 (0.0%)	0.04	97 (0.7%)	76 (0.5%)	0.03
Lab values- BUN (mg/dl); n (%)	1,874 (28.0%)	1,893 (28.3%)	-0.01	126 (1.7%)	116 (1.6%)	0.01	2,000 (14.3%)	2,009 (14.4%)	0.00
Lab values- BUN (mg/dl) (within 3 months); n (%)	1,255 (18.7%)	1,255 (18.7%)	0.00	75 (1.0%)	72 (1.0%)	0.00	1,330 (9.5%)	1,327 (9.5%)	0.00
Lab values- BUN (mg/dl) (within 6 months); n (%)	1,874 (28.0%)	1,893 (28.3%)	-0.01	126 (1.7%)	116 (1.6%)	0.01	2,000 (14.3%)	2,009 (14.4%)	0.00
Lab values- Creatinine (mg/dl) ; n (%)	1,936 (28.9%)	1,945 (29.0%)	0.00	140 (1.9%)	125 (1.7%)	0.02	2,076 (14.8%)	2,070 (14.8%)	0.00
Lab values- Creatinine (mg/dl) (within 3 months); n (%)	1,301 (19.4%)	1,295 (19.3%)	0.00	83 (1.1%)	81 (1.1%)	0.00	1,384 (9.9%)	1,376 (9.8%)	0.00
Lab values- Creatinine (mg/dl) (within 6 months); n (%)	1,936 (28.9%)	1,945 (29.0%)	0.00	140 (1.9%)	125 (1.7%)	0.02	2,076 (14.8%)	2,070 (14.8%)	0.00
Lab values- HDL level (mg/dl); n (%)	1,456 (21.7%)	1,486 (22.2%)	-0.01	118 (1.6%)	96 (1.3%)	0.03	1,574 (11.3%)	1,582 (11.3%)	0.00
Lab values- HDL level (mg/dl) (within 3 months); n (%)	890 (13.3%)	898 (13.4%)	0.00	58 (0.8%)	55 (0.8%)	0.00	0,948 (6.8%)	0,953 (6.8%)	0.00
Lab values- HDL level (mg/dl) (within 6 months); n (%)	1,456 (21.7%)	1,486 (22.2%)	-0.01	118 (1.6%)	96 (1.3%)	0.03	1,574 (11.3%)	1,582 (11.3%)	0.00
Lab values- LDL level (mg/dl) ; n (%)	1,496 (22.3%)	1,555 (23.2%)	-0.02	130 (1.8%)	102 (1.4%)	0.03	1,626 (11.6%)	1,657 (11.9%)	-0.01
Lab values- LDL level (mg/dl) (within 3 months); n (%)	911 (13.6%)	952 (14.2%)	-0.02	71 (1.0%)	61 (0.8%)	0.02	0,982 (7.0%)	1,013 (7.2%)	-0.01
Lab values- LDL level (mg/dl) (within 6 months); n (%)	1,496 (22.3%)	1,555 (23.2%)	-0.02	130 (1.8%)	102 (1.4%)	0.03	1,626 (11.6%)	1,657 (11.9%)	-0.01
Lab values- NT-proBNP; n (%)	12 (0.2%)	11 (0.2%)	0.00	0 (0.0%)	1 (0.0%)	#DIV/0!	12 (0.1%)	12 (0.1%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Lab values- NT-proBNP (within 3 months); n (%)	10 (0.1%)	7 (0.1%)	0.00	0 (0.0%)	1 (0.0%)	#DIV/0!	10 (0.1%)	8 (0.1%)	0.00
Lab values- NT-proBNP (within 6 months); n (%)	12 (0.2%)	11 (0.2%)	0.00	0 (0.0%)	1 (0.0%)	#DIV/0!	12 (0.1%)	12 (0.1%)	0.00
Lab values- Total cholesterol (mg/dl) ; n (%)	1,480 (22.1%)	1,514 (22.6%)	-0.01	116 (1.6%)	98 (1.3%)	0.03	1,596 (11.4%)	1,612 (11.5%)	0.00
Lab values- Total cholesterol (mg/dl) (within 3 months) ; n (%)	899 (13.4%)	912 (13.6%)	-0.01	58 (0.8%)	55 (0.8%)	0.00	0,957 (6.8%)	0,967 (6.9%)	0.00
Lab values- Total cholesterol (mg/dl) (within 6 months) ; n (%)	1,480 (22.1%)	1,514 (22.6%)	-0.01	116 (1.6%)	98 (1.3%)	0.03	1,596 (11.4%)	1,612 (11.5%)	0.00
Lab values- Triglyceride level (mg/dl); n (%)	1,453 (21.7%)	1,500 (22.4%)	-0.02	117 (1.6%)	94 (1.3%)	0.03	1,570 (11.2%)	1,594 (11.4%)	-0.01
Lab values- Triglyceride level (mg/dl) (within 3 months); n (%)	881 (13.2%)	906 (13.5%)	-0.01	57 (0.8%)	54 (0.7%)	0.01	0,938 (6.7%)	0,960 (6.9%)	-0.01
Lab values- Triglyceride level (mg/dl) (within 6 months); n (%)	1,453 (21.7%)	1,500 (22.4%)	-0.02	117 (1.6%)	94 (1.3%)	0.03	1,570 (11.2%)	1,594 (11.4%)	-0.01
Lab result number- HbA1c (%) mean (only 2 to 20 included)	1,398	1,379		123	100		0	0	
...mean (sd)	7.29 (1.75)	7.27 (1.76)	0.01	8.14 (1.81)	7.66 (1.81)	0.27	7.73 (1.78)	7.47 (1.79)	0.15
...median [IQR]	6.90 [6.00, 8.10]	6.75 [6.00, 8.00]	0.09	8.00 [6.80, 9.20]	7.18 [6.20, 8.95]	0.45	7.47 (1.78)	6.97 (1.79)	0.28
...Missing; n (%)	5,299 (79.1%)	5,318 (79.4%)	-0.01	7,160 (98.3%)	7,183 (98.6%)	-0.02	12,459 (89.1%)	12,501 (89.4%)	-0.01
Lab result number- BNP mean	87	74		10	2		0	0	
...mean (sd)	381.53 (1,230.47)	345.14 (679.13)	0.04	383.62 (605.09)	334.50 (0.71)	0.11	382.62 (957.10)	339.60 (470.04)	0.06
...median [IQR]	94.00 [42.00, 253.00]	94.50 [44.42, 276.17]	0.00	163.00 [86.75, 463.25]	334.50 [334.00, 335.00]	-0.40	129.95 (957.10)	219.53 (470.04)	-0.12
...Missing; n (%)	6,610 (98.7%)	6,623 (98.9%)	-0.02	7,273 (99.9%)	7,281 (100.0%)	-0.04	13,883 (99.3%)	13,904 (99.5%)	-0.03
Lab result number- BUN (mg/dl) mean	1,874	1,893		126	116		0	0	
...mean (sd)	18.97 (8.52)	18.95 (7.66)	0.00	1,128.51 (12,470.63)	3,361.89 (21,189.20)	-0.13	596.99 (9001.01)	1760.48 (15293.87)	-0.09
...median [IQR]	17.00 [14.00, 22.00]	17.00 [14.00, 22.00]	0.00	17.00 [14.00, 20.75]	17.00 [14.00, 21.00]	0.00	17.00 (9001.01)	17.00 (15293.87)	0.00
...Missing; n (%)	4,823 (72.0%)	4,804 (71.7%)	0.01	7,157 (98.3%)	7,167 (98.4%)	-0.01	11,980 (85.7%)	11,971 (85.6%)	0.00
Lab result number- Creatinine (mg/dl) mean (only 0.1 to 15 included)	1,913	1,927		121	103		2,034	2,030	
...mean (sd)	1.09 (0.45)	1.08 (0.40)	0.02	1.01 (0.23)	1.00 (0.24)	0.04	1.05 (0.35)	1.04 (0.33)	0.03
...median [IQR]	1.00 [0.84, 1.21]	1.00 [0.84, 1.22]	0.00	1.00 [0.86, 1.13]	1.00 [0.88, 1.12]	0.00	1.00 (0.35)	1.00 (0.33)	0.00
...Missing; n (%)	4,784 (71.4%)	4,770 (71.2%)	0.00	7,162 (98.3%)	7,180 (98.6%)	-0.02	11,946 (85.5%)	11,950 (85.5%)	0.00
Lab result number- HDL level (mg/dl) mean (only <=5000 included)	1,456	1,486		117	96		1,573	1,582	
...mean (sd)	46.40 (14.74)	46.63 (14.02)	-0.02	41.80 (11.50)	42.00 (12.11)	-0.02	44.00 (13.15)	44.22 (13.06)	-0.02
...median [IQR]	44.00 [36.00, 54.00]	44.00 [37.00, 54.00]	0.00	41.00 [33.50, 48.50]	41.00 [35.25, 48.00]	0.00	42.44 (13.15)	42.44 (13.06)	0.00
...Missing; n (%)	5,241 (78.3%)	5,211 (77.8%)	0.01	7,166 (98.4%)	7,187 (98.7%)	-0.03	12,407 (88.7%)	12,398 (88.7%)	0.00
Lab result number- LDL level (mg/dl) mean (only <=5000 included)	1,463	1,522		111	89		1,574	1,611	
...mean (sd)	101.93 (45.14)	103.69 (43.77)	-0.04	101.62 (50.86)	96.09 (46.22)	0.11	101.77 (48.20)	99.73 (45.06)	0.04
...median [IQR]	101.00 [75.00, 128.00]	100.00 [75.00, 131.00]	0.02	99.00 [69.00, 134.50]	104.50 [61.00, 129.00]	-0.11	99.96 (48.20)	102.34 (45.06)	-0.05
...Missing; n (%)	5,234 (78.2%)	5,175 (77.3%)	0.02	7,172 (98.5%)	7,194 (98.8%)	-0.03	12,406 (88.7%)	12,369 (88.5%)	0.01

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Lab result number- Total cholesterol (mg/dl) mean (only <=5000 included)	1,476	1,510		115	97		1,591	1,607	
...mean (sd)	188.01 (53.70)	187.17 (49.11)	0.02	190.24 (53.63)	187.50 (45.93)	0.05	189.17 (53.66)	187.34 (47.48)	0.04
...median [IQR]	183.00 [153.00, 214.00]	182.00 [154.00, 216.00]	0.02	197.00 [148.50, 230.00]	186.00 [156.50, 219.25]	0.22	190.29 (53.66)	184.08 (47.48)	0.12
...Missing; n (%)	5,221 (78.0%)	5,187 (77.5%)	0.01	7,168 (98.4%)	7,186 (98.7%)	-0.03	12,389 (88.6%)	12,373 (88.5%)	0.00
Lab result number- Triglyceride level (mg/dl) mean (only <=5000 included)	1,450	1,500		116	93		1,566	1,593	
...mean (sd)	178.04 (146.67)	171.98 (120.25)	0.05	191.07 (122.18)	207.13 (136.39)	-0.12	184.83 (134.47)	190.29 (128.91)	-0.04
...median [IQR]	143.00 [104.00, 209.25]	143.50 [104.00, 203.88]	0.00	163.50 [103.12, 239.50]	165.00 [122.00, 245.00]	-0.01	153.68 (134.47)	154.70 (128.91)	-0.01
...Missing; n (%)	5,247 (78.3%)	5,197 (77.6%)	0.02	7,167 (98.4%)	7,190 (98.7%)	-0.03	12,414 (88.8%)	12,387 (88.6%)	0.01
Lab result number- Hemoglobin mean (only >0 included)	1,451	1,430		97	75		1,548	1,505	
...mean (sd)	13.81 (1.81)	13.82 (1.78)	-0.01	13.82 (2.15)	135,417.06 (1,154,595.69)	-0.17	13.82 (1.99)	70553.29 (833360.19)	-0.12
...median [IQR]	13.90 [12.60, 15.10]	14.00 [12.60, 15.01]	-0.06	14.00 [12.80, 15.30]	14.10 [13.00, 15.00]	0.00	13.95 (1.99)	14.05 (833360.19)	0.00
...Missing; n (%)	5,246 (78.3%)	5,267 (78.6%)	-0.01	7,186 (98.7%)	7,208 (99.0%)	-0.03	12,432 (88.9%)	12,475 (89.2%)	-0.01
Lab result number- Serum sodium mean (only > 90 and < 190 included)	1,869	1,891		133	111		2,002	2,002	
...mean (sd)	139.98 (2.88)	140.05 (2.79)	-0.02	138.91 (2.64)	139.51 (2.55)	-0.23	139.42 (2.76)	139.77 (2.67)	-0.13
...median [IQR]	140.00 [138.33, 142.00]	140.00 [138.50, 142.00]	0.00	139.00 [137.00, 141.00]	140.00 [138.00, 141.00]	-0.39	139.48 (2.76)	140.00 (2.67)	-0.19
...Missing; n (%)	4,828 (72.1%)	4,806 (71.8%)	0.01	7,150 (98.2%)	7,172 (98.5%)	-0.02	11,978 (85.7%)	11,978 (85.7%)	0.00
Lab result number- Albumin mean (only >0 and <=10 included)	1,708	1,714		115	94		1,823	1,808	
...mean (sd)	4.19 (0.35)	4.20 (0.34)	-0.03	4.11 (0.54)	4.04 (0.45)	0.14	4.15 (0.46)	4.12 (0.40)	0.07
...median [IQR]	4.20 [4.00, 4.40]	4.20 [4.00, 4.40]	0.00	4.10 [4.00, 4.40]	4.00 [4.00, 4.40]	0.20	4.15 (0.46)	4.10 (0.40)	0.12
...Missing; n (%)	4,989 (74.5%)	4,983 (74.4%)	0.00	7,168 (98.4%)	7,189 (98.7%)	-0.03	12,157 (87.0%)	12,172 (87.1%)	0.00
Lab result number- Glucose (fasting or random) mean (only 10-1000 included)	1,858	1,885		133	113		1,991	1,998	
...mean (sd)	135.97 (63.19)	134.68 (61.29)	0.02	167.91 (62.54)	152.10 (61.99)	0.25	152.61 (62.85)	143.76 (61.66)	0.14
...median [IQR]	114.00 [96.00, 156.00]	113.00 [97.00, 151.00]	0.02	153.00 [119.50, 202.00]	139.00 [110.33, 179.80]	0.22	134.32 (62.85)	126.54 (61.66)	0.12
...Missing; n (%)	4,839 (72.3%)	4,812 (71.9%)	0.01	7,150 (98.2%)	7,170 (98.4%)	-0.02	11,989 (85.8%)	11,982 (85.7%)	0.00
Lab result number- Potassium mean (only 1-7 included)	1,914	1,926		124	108		2,038	2,034	
...mean (sd)	4.44 (0.44)	4.46 (0.44)	-0.05	4.29 (0.48)	4.16 (0.44)	0.28	4.36 (0.46)	4.30 (0.44)	0.13
...median [IQR]	4.40 [4.15, 4.70]	4.40 [4.20, 4.70]	0.00	4.29 [4.00, 4.60]	4.10 [4.00, 4.40]	0.41	4.34 (0.46)	4.24 (0.44)	0.22
...Missing; n (%)	4,783 (71.4%)	4,771 (71.2%)	0.00	7,159 (98.3%)	7,175 (98.5%)	-0.02	11,942 (85.4%)	11,946 (85.5%)	0.00
Comorbidity Scores									
CCI (180 days)- ICD9 and ICD10									
...mean (sd)	3.71 (2.43)	3.71 (2.43)	0.00	2.24 (1.64)	2.24 (1.64)	0.00	2.94 (2.06)	2.94 (2.06)	0.00
...median [IQR]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	0.00	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	0.00	2.48 (2.06)	2.48 (2.06)	0.00
Frailty Score (mean): Empirical Version 365 days,									
...mean (sd)	0.20 (0.05)	0.20 (0.05)	0.00	0.18 (0.04)	0.18 (0.04)	0.00	0.19 (0.05)	0.19 (0.05)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...median [IQR]	0.19 [0.16, 0.22]	0.19 [0.16, 0.22]	0.00	0.17 [0.15, 0.19]	0.17 [0.15, 0.19]	0.00	0.18 (0.05)	0.18 (0.05)	0.00
Healthcare Utilization									
Any hospitalization; n (%)	6,686 (99.8%)	6,690 (99.9%)	-0.03	7,283 (100.0%)	7,283 (100.0%)	#DIV/0!	13,969 (99.9%)	13,973 (99.9%)	0.00
Any hospitalization during prior 31-180 days; n (%)	336 (5.0%)	411 (6.1%)	-0.05	176 (2.4%)	192 (2.6%)	-0.01	0,512 (3.7%)	0,603 (4.3%)	-0.03
Endocrinologist Visit; n (%)	464 (6.9%)	450 (6.7%)	0.01	405 (5.6%)	390 (5.4%)	0.01	0,869 (6.2%)	0,840 (6.0%)	0.01
Endocrinologist Visit (30 days prior); n (%)	239 (3.6%)	227 (3.4%)	0.01	198 (2.7%)	210 (2.9%)	-0.01	0,437 (3.1%)	0,437 (3.1%)	0.00
Endocrinologist Visit (31 to 180 days prior); n (%)	294 (4.4%)	294 (4.4%)	0.00	253 (3.5%)	234 (3.2%)	0.02	0,547 (3.9%)	0,528 (3.8%)	0.01
Internal medicine/family medicine visits; n (%)	5,736 (85.7%)	5,717 (85.4%)	0.01	5,239 (71.9%)	5,227 (71.8%)	0.00	10,975 (78.5%)	10,944 (78.3%)	0.00
Internal medicine/family medicine visits (30 days prior) ; n (%)	4,788 (71.5%)	4,783 (71.4%)	0.00	3,320 (45.6%)	3,241 (44.5%)	0.02	8,108 (58.0%)	8,024 (57.4%)	0.01
Internal medicine/family medicine visits (31 to 180 days prior) ; n (%)	4,341 (64.8%)	4,335 (64.7%)	0.00	4,170 (57.3%)	4,231 (58.1%)	-0.02	8,511 (60.9%)	8,566 (61.3%)	-0.01
Cardiologist visit; n (%)	6,365 (95.0%)	6,231 (93.0%)	0.08	2,849 (39.1%)	2,776 (38.1%)	0.02	9,214 (65.9%)	9,007 (64.4%)	0.03
Number of Cardiologist visits (30 days prior); n (%)	6,321 (94.4%)	6,192 (92.5%)	0.08	2,372 (32.6%)	2,275 (31.2%)	0.03	8,693 (62.2%)	8,467 (60.6%)	0.03
Number of Cardiologist visits (31 to 180 days prior); n (%)	1,442 (21.5%)	1,466 (21.9%)	-0.01	923 (12.7%)	952 (13.1%)	-0.01	2,365 (16.9%)	2,418 (17.3%)	-0.01
Electrocardiogram ; n (%)	6,294 (94.0%)	6,275 (93.7%)	0.01	4,153 (57.0%)	4,022 (55.2%)	0.04	10,447 (74.7%)	10,297 (73.7%)	0.02
Use of glucose test strips; n (%)	121 (1.8%)	127 (1.9%)	-0.01	106 (1.5%)	102 (1.4%)	0.01	0,227 (1.6%)	0,229 (1.6%)	0.00
Dialysis; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!
number of different/distinct medication prescriptions									
...mean (sd)	10.48 (5.17)	10.46 (5.10)	0.00	9.41 (4.44)	9.33 (4.38)	0.02	9.92 (4.80)	9.87 (4.74)	0.01
...median [IQR]	10.00 [7.00, 13.00]	10.00 [7.00, 13.00]	0.00	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	0.00	9.48 (4.80)	9.48 (4.74)	0.00
Number of Hospitalizations									
...mean (sd)	1.13 (0.42)	1.13 (0.44)	0.00	1.06 (0.27)	1.06 (0.27)	0.00	1.09 (0.35)	1.09 (0.36)	0.00
...median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.00	1.00 (0.35)	1.00 (0.36)	0.00
Number of hospital days									
...mean (sd)	4.37 (3.32)	4.42 (3.60)	-0.01	3.62 (2.00)	3.64 (2.13)	-0.01	3.98 (2.71)	4.01 (2.93)	-0.01
...median [IQR]	3.00 [3.00, 5.00]	3.00 [3.00, 5.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 (2.71)	3.00 (2.93)	0.00
Number of Emergency Department (ED) visits									
...mean (sd)	1.18 (1.53)	1.19 (1.76)	-0.01	3.37 (5.61)	3.33 (5.97)	0.01	2.32 (4.19)	2.30 (4.48)	0.00
...median [IQR]	1.00 [0.00, 2.00]	1.00 [0.00, 1.00]	0.00	2.00 [0.00, 4.00]	2.00 [0.00, 4.00]	0.00	1.52 (4.19)	1.52 (4.48)	0.00
Number of Office visits									
...mean (sd)	4.04 (3.89)	4.00 (3.76)	0.01	3.12 (3.28)	3.09 (3.24)	0.01	3.56 (3.59)	3.53 (3.50)	0.01
...median [IQR]	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	0.00	2.00 [1.00, 4.00]	2.00 [1.00, 4.00]	0.00	2.48 (3.59)	2.48 (3.50)	0.00
Number of Endocrinologist visits									
...mean (sd)	0.29 (1.73)	0.30 (1.91)	-0.01	0.22 (1.30)	0.23 (1.48)	-0.01	0.68 (1.41)	0.69 (1.62)	-0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.48 (1.41)	0.48 (1.62)	0.00
Number of internal medicine/family medicine visits									
...mean (sd)	9.83 (13.95)	9.77 (13.26)	0.00	4.68 (7.55)	4.58 (7.32)	0.01	7.15 (11.09)	7.07 (10.59)	0.01
...median [IQR]	6.00 [2.00, 12.00]	6.00 [2.00, 12.00]	0.00	2.00 [0.00, 6.00]	2.00 [0.00, 6.00]	0.00	3.92 (11.09)	3.92 (10.59)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

Number of Cardiologist visits									
...mean (sd)	9.71 (7.61)	9.65 (6.80)	0.01	1.28 (2.49)	1.30 (2.66)	-0.01	5.32 (5.57)	5.30 (5.08)	0.00
...median [IQR]	9.00 [6.00, 12.00]	9.00 [6.00, 12.00]	0.00	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.00	4.31 (5.57)	4.31 (5.08)	0.00
Number electrocardiograms received									
...mean (sd)	3.62 (3.22)	3.57 (3.02)	0.02	1.13 (1.46)	1.10 (1.48)	0.02	2.32 (2.47)	2.28 (2.35)	0.02
...median [IQR]	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	0.00	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	0.00	1.96 (2.47)	1.96 (2.35)	0.00
Number of HbA1c tests ordered									
...mean (sd)	0.56 (0.81)	0.55 (0.79)	0.01	0.34 (0.66)	0.32 (0.63)	0.03	0.45 (0.74)	0.43 (0.71)	0.03
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.74)	0.00 (0.71)	0.00
Number of glucose tests ordered									
...mean (sd)	0.27 (1.06)	0.31 (2.85)	-0.02	0.14 (0.58)	0.16 (0.99)	-0.02	0.20 (0.84)	0.23 (2.10)	-0.02
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.84)	0.00 (2.10)	0.00
Number of lipid tests ordered									
...mean (sd)	0.61 (0.81)	0.61 (0.80)	0.00	0.44 (0.88)	0.43 (0.85)	0.01	0.52 (0.85)	0.52 (0.83)	0.00
...median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00	0.00 (0.85)	0.00 (0.83)	0.00
Number of creatinine tests ordered									
...mean (sd)	0.06 (0.29)	0.06 (0.34)	0.00	0.04 (0.24)	0.04 (0.23)	0.00	0.05 (0.27)	0.05 (0.29)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.27)	0.00 (0.29)	0.00
Number of BUN tests ordered									
...mean (sd)	0.03 (0.22)	0.04 (0.27)	-0.04	0.02 (0.16)	0.02 (0.17)	0.00	0.02 (0.19)	0.03 (0.22)	-0.05
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.19)	0.00 (0.22)	0.00
Number of tests for microalbuminuria									
...mean (sd)	0.33 (0.81)	0.33 (0.81)	0.00	0.17 (0.58)	0.15 (0.54)	0.04	0.25 (0.70)	0.24 (0.68)	0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.70)	0.00 (0.68)	0.00
Total N distinct ICD9/ICD10 diagnoses at the 3rd digit level									
...mean (sd)	13.25 (11.46)	13.42 (11.51)	-0.01	7.61 (8.40)	7.68 (8.58)	-0.01	10.31 (9.98)	10.43 (10.09)	-0.01
...median [IQR]	12.00 [4.00, 19.00]	12.00 [4.00, 20.00]	0.00	4.00 [0.00, 14.00]	4.00 [0.00, 14.00]	0.00	7.83 (9.98)	7.83 (10.09)	0.00
For PS									
Hemorrhagic stroke+Other cerebrovascular disease+Cerebrovascular procedure (for PS); n (%)	155 (2.3%)	163 (2.4%)	-0.01	78 (1.1%)	77 (1.1%)	0.00	233 (1.7%)	240 (1.7%)	0.00
Occurrence of creatinine tests ordered (for PS); n (%)	299 (4.5%)	291 (4.3%)	0.01	204 (2.8%)	211 (2.9%)	-0.01	0,503 (3.6%)	0,502 (3.6%)	0.00
Occurrence of BUN tests ordered (for PS); n (%)	168 (2.5%)	167 (2.5%)	0.00	115 (1.6%)	117 (1.6%)	0.00	0,283 (2.0%)	0,284 (2.0%)	0.00
Occurrence of chronic renal insufficiency w/o CKD (for PS) ; n (%)	704 (10.5%)	682 (10.2%)	0.01	244 (3.4%)	229 (3.1%)	0.02	0,948 (6.8%)	0,911 (6.5%)	0.01
Chronic kidney disease Stage 1-2 (for PS); n (%)	290 (4.3%)	267 (4.0%)	0.02	72 (1.0%)	72 (1.0%)	0.00	362 (2.6%)	339 (2.4%)	0.01
Chronic kidney disease Stage 3-6 (for PS); n (%)	1,070 (16.0%)	1,060 (15.8%)	0.01	340 (4.7%)	337 (4.6%)	0.00	1,410 (10.1%)	1,397 (10.0%)	0.00
Bladder stones+Kidney stones (for PS); n (%)	224 (3.3%)	209 (3.1%)	0.01	133 (1.8%)	122 (1.7%)	0.01	0,357 (2.6%)	0,331 (2.4%)	0.01
Diabetes with peripheral circulatory disorders+Gangrene+Osteomyelitis(for PS) with ICD10 ; n (%)	464 (6.9%)	464 (6.9%)	0.00	147 (2.0%)	144 (2.0%)	0.00	0,611 (4.4%)	0,608 (4.3%)	0.00

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...mean (sd)	1,800.74 (1,442.20)	1,791.98 (1,450.03)	0.01	2,250.83 (1,484.36)	2,264.37 (1,484.25)	-0.01	2035.22 (1464.32)	2038.08 (1467.96)	0.00
...median [IQR]	1,342.00 [646.00, 2,614.00]	1,327.00 [641.50, 2,621.50]	0.01	1,996.00 [941.00, 3,521.00]	1,990.00 [966.00, 3,538.00]	0.00	1682.71 (1464.32)	1672.40 (1467.96)	0.01
Mean Copay for per prescription cost (charges in U.S. \$) (180-1 day prior)									
...mean (sd)	22.65 (29.77)	22.98 (32.80)	-0.01	16.54 (20.34)	16.64 (21.51)	0.00	19.47 (25.30)	19.68 (27.50)	-0.01
...median [IQR]	13.37 [5.00, 30.00]	13.80 [5.01, 29.28]	-0.01	10.61 [2.74, 23.07]	10.96 [3.67, 22.35]	-0.02	11.93 (25.30)	12.32 (27.50)	-0.01
...Missing; n (%)	579 (8.6%)	581 (8.7%)	0.00	850 (11.7%)	891 (12.2%)	-0.02	1,429 (10.2%)	1472 (10.5%)	-0.01
Colonos; n (%)	254 (3.8%)	266 (4.0%)	-0.01	263 (3.6%)	250 (3.4%)	0.01	0,517 (3.7%)	516 (3.7%)	0.00
Fecal occult blood (FOB) test; n (%)	196 (2.9%)	192 (2.9%)	0.00	160 (2.2%)	164 (2.3%)	-0.01	0,356 (2.5%)	356 (2.5%)	0.00
Flu vaccine; n (%)	974 (14.5%)	1,032 (15.4%)	-0.03	646 (8.9%)	637 (8.7%)	0.01	1,620 (11.6%)	1669 (11.9%)	-0.01
Mammogram; n (%)	422 (6.3%)	439 (6.6%)	-0.01	277 (3.8%)	298 (4.1%)	-0.02	0,699 (5.0%)	737 (5.3%)	-0.01
Pap smear; n (%)	104 (1.6%)	103 (1.5%)	0.01	118 (1.6%)	125 (1.7%)	-0.01	0,222 (1.6%)	228 (1.6%)	0.00
Pneumonia vaccine; n (%)	1,207 (18.0%)	1,261 (18.8%)	-0.02	624 (8.6%)	622 (8.5%)	0.00	1,831 (13.1%)	1883 (13.5%)	-0.01
PSA test or Prostate exam for DRE; n (%)	963 (14.4%)	952 (14.2%)	0.01	792 (10.9%)	802 (11.0%)	0.00	1,755 (12.6%)	1754 (12.5%)	0.00
Bone mineral density; n (%)	157 (2.3%)	163 (2.4%)	-0.01	79 (1.1%)	78 (1.1%)	0.00	0,236 (1.7%)	241 (1.7%)	0.00
Use of Sympatomimetic agents; n (%)	38 (0.6%)	43 (0.6%)	0.00	79 (1.1%)	80 (1.1%)	0.00	0,117 (0.8%)	123 (0.9%)	-0.01
Use of CNS stimulants; n (%)	17 (0.3%)	23 (0.3%)	0.00	38 (0.5%)	42 (0.6%)	-0.01	0,055 (0.4%)	65 (0.5%)	-0.01
Use of estrogens, progestins, androgens; n (%)	204 (3.0%)	180 (2.7%)	0.02	287 (3.9%)	298 (4.1%)	-0.01	0,491 (3.5%)	478 (3.4%)	0.01
Use of Angiogenesis inhibitors; n (%)	8 (0.1%)	5 (0.1%)	0.00	0 (0.0%)	1 (0.0%)	#DIV/0!	0,008 (0.1%)	6 (0.0%)	0.04
Use of Oral Immunosuppressants; n (%)	16 (0.2%)	15 (0.2%)	0.00	22 (0.3%)	19 (0.3%)	0.00	0,038 (0.3%)	34 (0.2%)	0.02
Use of fondaparinux or Bivalirudin; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0 (0.0%)	#DIV/0!
Use of other direct thrombin inhibitors (lepirudin, desirudin, argatroban); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	0,000 (0.0%)	0 (0.0%)	#DIV/0!
Use of Prasugrel ON CED; n (%)	22 (0.3%)	29 (0.4%)	-0.02	34 (0.5%)	33 (0.5%)	0.00	0,056 (0.4%)	62 (0.4%)	0.00
Use of Prasugrel 180 to 1 day prior; n (%)	47 (0.7%)	61 (0.9%)	-0.02	56 (0.8%)	52 (0.7%)	0.01	0,103 (0.7%)	113 (0.8%)	-0.01
Duration of index hospitalization (i.e. anchor hospitalization LOS)									
...mean (sd)	3.97 (2.97)	4.01 (3.08)	-0.01	3.40 (1.60)	3.43 (1.62)	-0.02	3.67 (2.36)	3.71 (2.43)	-0.02
...median [IQR]	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 [2.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.00 (2.36)	3.00 (2.43)	0.00
Number of D-dimer tests									
...mean (sd)	0.04 (0.22)	0.04 (0.23)	0.00	0.05 (0.24)	0.06 (0.26)	-0.04	0.05 (0.23)	0.05 (0.25)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.23)	0.00 (0.25)	0.00
Numbe of CRP, high-sensitivity CRP tests									
...mean (sd)	0.06 (0.31)	0.06 (0.31)	0.00	0.04 (0.27)	0.04 (0.26)	0.00	0.05 (0.29)	0.05 (0.29)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.29)	0.00 (0.29)	0.00
Number of PT or aPTT tests									
...mean (sd)	0.41 (1.41)	0.41 (1.40)	0.00	0.39 (0.97)	0.38 (1.01)	0.01	0.40 (1.20)	0.39 (1.21)	0.01
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (1.20)	0.00 (1.21)	0.00
Number of Bleeding time tests									
...mean (sd)	0.00 (0.04)	0.00 (0.02)	0.00	0.00 (0.01)	0.00 (0.01)	0.00	0.00 (0.03)	0.00 (0.02)	0.00
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.00	0.00 (0.03)	0.00 (0.02)	0.00
HAS-BLED Score (ICD-9 and ICD-10), 180 days									
...mean (sd)	3.91 (0.75)	3.92 (0.74)	-0.01	3.40 (0.61)	3.40 (0.60)	0.00	3.64 (0.68)	3.65 (0.67)	-0.01

Table 1: Ticagrelor 90 mg vs Clopidogrel 75 mg

...median [IQR]	4.00 [3.00, 4.00]	4.00 [3.00, 4.00]	0.00	3.00 [3.00, 4.00]	3.00 [3.00, 4.00]	0.00	3.48 (0.68)	3.48 (0.67)	0.00
Drug eluting stent; n (%)	1,231 (18.4%)	1,211 (18.1%)	0.01	2,311 (31.7%)	2,256 (31.0%)	0.02	3,542 (25.3%)	3467 (24.8%)	0.01
Bare metal stent; n (%)	5,572 (83.2%)	5,570 (83.2%)	0.00	6,125 (84.1%)	6,043 (83.0%)	0.03	11,697 (83.7%)	11613 (83.1%)	0.02
Use of CYP inhibitors; n (%)	1,377 (20.6%)	1,380 (20.6%)	0.00	1,243 (17.1%)	1,220 (16.8%)	0.01	2,620 (18.7%)	2600 (18.6%)	0.00
Use of CYP inducers; n (%)	7 (0.1%)	6 (0.1%)	0.00	10 (0.1%)	8 (0.1%)	0.00	0,017 (0.1%)	14 (0.1%)	0.00
Commercial vs Medicare Advantage- Business Type Code - CORRECT ONE - TRUVEN									
...Commercial; n (%)	1,994 (29.8%)	1,995 (29.8%)	0.00	2,433 (33.4%)	2,455 (33.7%)	-0.01	4,427 (31.7%)	4450 (31.8%)	0.00
...Medicare Advantage; n (%)	4,703 (70.2%)	4,702 (70.2%)	0.00	4,850 (66.6%)	4,828 (66.3%)	0.01	9,553 (68.3%)	9530 (68.2%)	0.00
Commercial vs Medicare Advantage- Business Type Code									
...COM = COMMERCIAL; n (%)	1,994 (29.8%)	1,995 (29.8%)	0.00	-	-	#VALUE!	1,994 (29.8%)	1,995 (29.8%)	0.00
...MCR = MEDICARE; n (%)	4,703 (70.2%)	4,702 (70.2%)	0.00	-	-	#VALUE!	4,703 (70.2%)	4,702 (70.2%)	0.00
...MCD = MEDICAID; n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...NONE = NO BUSINESS LINE CODE (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
...UNK = UNKNOWN (added in 2015); n (%)	0 (0.0%)	0 (0.0%)	#DIV/0!	-	-	#VALUE!	0 (0.0%)	0 (0.0%)	#DIV/0!
Commercial vs Medicare Advantage- Data Type									
...1 - Fee For Service; n (%)	-	-	#VALUE!	4,383 (60.2%)	4,356 (59.8%)	0.01	4,383 (60.2%)	4,356 (59.8%)	0.01
...2 - Encounter; n (%)	-	-	#VALUE!	467 (6.4%)	472 (6.5%)	0.00	467 (6.4%)	472 (6.5%)	0.00
...3 - Medicare; n (%)	-	-	#VALUE!	2,169 (29.8%)	2,198 (30.2%)	-0.01	2,169 (29.8%)	2,198 (30.2%)	-0.01
...4 - Medicare Encounter; n (%)	-	-	#VALUE!	264 (3.6%)	257 (3.5%)	0.01	264 (3.6%)	257 (3.5%)	0.01
Metropolitan Statistical Area - Urban (any MSA) vs Rural (non-MSA)									
...Urban; n (%)	-	-	#VALUE!	5,129 (70.4%)	5,146 (70.7%)	-0.01	5,129 (70.4%)	5,146 (70.7%)	-0.01
...Rural; n (%)	-	-	#VALUE!	559 (7.7%)	533 (7.3%)	0.02	559 (7.7%)	533 (7.3%)	0.02
...Unknown/Missing; n (%)	-	-	#VALUE!	1,595 (21.9%)	1,604 (22.0%)	0.00	1,595 (21.9%)	1,604 (22.0%)	0.00
N of Generic name drugs									
...mean (sd)	16.07 (12.36)	15.97 (13.43)	0.01	12.49 (8.99)	12.30 (9.86)	0.020138	14.20 (10.74)	14.06 (11.71)	0.01
...median [IQR]	13.00 [8.00, 21.00]	13.00 [7.00, 21.00]	0.00	10.00 [6.00, 16.00]	10.00 [5.00, 16.00]	0	11.44 (10.74)	11.44 (11.71)	0.00
N of Brand name drugs									
...mean (sd)	3.76 (5.67)	3.73 (4.17)	0.01	3.65 (5.13)	3.63 (3.53)	0.00	3.70 (5.40)	3.68 (3.85)	0.07
...median [IQR]	1.00 [0.00, 5.00]	2.00 [1.00, 5.00]	-0.20	2.00 [0.00, 5.00]	2.00 [1.00, 5.00]	0	1.52 (5.40)	2.00 (3.85)	0.07